HEALTH AND ENVIRONMENTAL FACTORS

FUNGICIDE ASSESSMENT

National Agricultural Pesticide Impact Assessment Program (NAPIAP)

HEALTH AND ENVIRONMENTAL FACTORS ASSOCIATED WITH AGRICULTURAL USE OF FUNGICIDES

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This Report Represents A Portion Of The USDA/States National Agricultural Pesticide Impact Assessment Program (NAPIAP) Fungicide Assessment Project.

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PREFACE

Fungicides are essential for the health of plants, animals and mankind. The term "fungicide" is primarily used in conjunction with the agricultural application of these chemicals to control or reduce incidence of plant infections resulting from disease-causing fungi. These chemical uses are registered by the U.S. Environmental Protection Agency. When similar chemicals are used for animal and human fungal infections, "antifungal drug" seems to be the term of choice. These drugs are approved for use by the U.S. Food and Drug Administration. Although the principles of activity are identical, end use appears to determine public views of chemicals used to control fungi.

This treatise focuses on the agricultural use of fungicides and examines factors that should be taken into consideration when regulatory decisions are made that affect these uses. This represents a segment of the USDA / States National Agricultural Pesticide Impact Assessment Program's Fungicide Assessment Project. There are two other parts: a fungicide benefits assessment report which examines the impact of these chemicals on agricultural production, and an assessment of the status as well as the management strategies for fungal resistance to fungicides in the United States.

The preparation of material for this document was executed in several stages. An initial report was prepared through a cooperative agreement between the University of California at Davis and the Cooperative State Research Service, USDA. James N. Seiber of the University of California served as the project director. The report itself, which provided a vast amount of information on fungicides as well as pesticides in general and their relation to health and the environment, was prepared through the Department of Environmental Toxicology and the Cooperative Extension Service at Davis. Those who contributed were (in alphabetical order):

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This report, which was entitled "Review of Agricultural Fungicides: Food Residues, Environmental Fates, Risks, Benefits, and Health Effects," was reviewed in depth by a panel of distinguished scientists representing academia, federal and state governments, food processors and the pesticide industry. Serving on this panel were the following:

Hugh Sisler, Panel Chairman
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Based upon the panel's review and other relevant data, the editor and associate editors made extensive revisions and additions to the original report and thus developed this current treatise.

We would like to express our appreciation to all who had a role in developing this material. We would like to recognize Ann Orth, Pennsylvania State University, for her critical review of the original report; Christopher Wilkinson, Risk Focus (Div. of Versar), for his helpful suggestions regarding the discussion of risk assessment; and George Fong, Florida Department of Agriculture and Consumer Services, for information on residue analyses. We would especially like to thank Harold Alford and Linda Herbst of the University of California, Davis, as well as Iris Dean and Patty Nitowitz of the University of Maryland for their extensive efforts involved in the panel review and preparation of the final report.

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EXECUTIVE SUMMARY

CHAPTER 1 –
Overview of Fungicides

- Without fungicides there would be devastating crop failures, higher food prices and a striking increase of fungal contaminated food. The ability to export food from local production areas to domestic and international markets would be severely curtailed.
- All economically important plants are subject to attack by one or more fungal species. Often 10 to 50 different fungi may cause disease of one plant species. Different parts of the country have different needs for disease control chemicals as a result of the prevailing weather conditions, which affect fungal species present.
- The wide variations in fungi which cause diseases require a correspondingly varied arsenal of fungicides. The phenomenon of biological activity of fungicides is very complex and knowledge of the processes involved is limited. Further advances in the chemical control of fungal diseases will depend to a large degree on a better understanding of the factors which control the selective action of a compound.
- A farmer is not likely to use a particular fungicide unless the benefits (e.g., prevention of crop loss, destruction of fungi producing a health hazard, and improved quality) exceed the costs

of applying it. Since many products compete with each other, cost and effectiveness are factors determining which fungicides are used.

- The older fungicides include inorganic compounds (such as copper and sulfur) and organic surface protectants (such as thiram, captan, maneb and chlorothalonil). These compounds act only at the surface of the plant and must be present at or before appearance of the fungal pathogen in order to prevent infection. These older fungicides are multisite inhibitors (i.e., they affect many metabolic activities in a fungus).

- Most of the newer fungicides are highly effective organic systemics (such as the benzimidazoles, sterol biosynthesis inhibitors, carboxanilides and phenylamides) that act internally as well as at the plant surface. In contrast to the older sulface protectants, the systemic fungicides are generally effective at much lower dosages and can cure established fungal infections, a critical factor in disease management. The systemic fungicides usually act at a single target site in the fungus interfering with specific metabolic processes that are necessary for production of new cell material required for growth, maintenance and virulence of the fungal organism.

- The high degree of specificity in the systemic fungicides has led to serious problems with fungal resistance; thus, resistance management programs are essential for their successful use. Preventing or delaying resistance may require rotating fungicides or applying mixtures of fungicides with differing modes of action. In either case, it is necessary that a variety of fungicides be available (i.e. registered) for each commodity.

- Regulatory authorities should understand that canceling the use of older surface-protectant fungicides that are not subject to serious problems with pathogen resistance will almost certainly result in much more serious fungal resistance problems for systemic fungicides.

- The principles of integrated pest management (IPM) have been practiced for the control of plant diseases for many years before the phrase was coined. The use of immune or highly resistant (to disease-causing organisms) plant varieties, crop rotation, pruning and burning diseased parts, modifying post-harvest handling techniques and storage conditions and enforcing strict quarantine regulations are examples of non-fungicidal measures that reduce chances of disease occurrence. Fungicide application is an integral part of most successful IPM programs. For the near term there are

no apparent new strategies that depart from those currently in practice. Because the possibility always exists that disease-causing fungi will break through non-chemical defenses, fungicides are absolutely essential.

CHAPTER 2 – *Advantages to the Public from the Use of Fungicides*

- Producers as well as consumers benefit from the use of fungicides. The prevention of yield losses, improved crop quality, enhanced market opportunities, facilitation of farmwork and harvest, and improvement of the cost/profit ratio serve the farmer well. The advantage for the consumer is an ample, varied, safe, healthy and inexpensive food supply available throughout the year.
- The role that fungicides play in preventing food contamination with toxic fungal products (mycotoxins) and plant defense chemicals (phytoalexins) is not widely recognized. Since we have information on the toxicological hazards of only a few of the hundreds of agriculturally significant fungi, the safest course to follow is to prevent fungal infections or contaminations of food products whenever possible. Studies indicate that in addition to controlling fungi, effective insect management is necessary since insect vectors carry fungi internally and externally and thus are culprits in fungal infection.
- Foods can become contaminated with mycotoxins produced by fungi in the field, after harvest, in storage, or during processing. Mycotoxins include fungal products which are carcinogens, nerve poisons, liver and kidney poisons, to name a few. Patulin, tenuazonic acid, aflatoxins and ergot toxins are well known examples of these fungal products.
- Plants are equipped to protect themselves against predators and pests primarily through chemical defense mechanisms. Many plants, upon contact with a pathogenic or non-pathogenic fungus, form antifungal compounds called phytoalexins. Phytoalexins inhibit growth or cause premature death of fungi and are toxic to many other biological species including animals and humans. Among the better known plant defense chemicals are pisatin, ipomeamarone and xanthotoxin. It has been suggested that insects and diseases be warded off by developing resistant crop varieties on the basis of their ability to accumulate chemicals toxic to pests. However, one must realize that excessive induction of such chemicals in a plant may cause phytotoxicity and also lead to other undesirable side-effects such as human and animal poisonings.

- Banning the use of a fungicide causing a very small risk may expose the public to fungal food contamination presenting much greater risks due to mycotoxins and fungal induced phytoalexins. Responsible regulation of fungicide uses calls for balancing the risks.

CHAPTER 3 –
Behavior of Fungicide Residues in the Environment

- Fungicide residues are not very persistent, a factor directly related to the physical and chemical characteristics of these compounds. As a result, they are seldom found in random environmental sampling of the air, water and biota. This, coupled with their generally low non-target toxicity and relatively low use in comparison to herbicides and insecticides, is the reason why fungicides have not been as actively sought in environmental monitoring programs as some other pesticides.
- Fungicides may be toxic to many microorganisms and thus must be used judiciously in pest management programs that include beneficial control organisms.
- The persistence of fungicide residues in soil is influenced by many complex, related factors such as rate and manner of application (including factors such as formulation), and the extreme variability of local conditions. Microbial degradation may be the single most important factor in preventing the buildup of fungicide residues. In some circumstances these residues may be degraded so rapidly that their effectiveness is greatly reduced or even eliminated; this phenomenon is known as "enhanced" or "accelerated" microbial degradation.
- The ultimate fates of many fungicides and their residues have not been fully determined nor has the chronic environmental toxicity been evaluated. However, the data that exist, together with the lack of evidence suggesting detrimental impacts, indicate that this is not a priority area for concern.

CHAPTER 4 –
Fungicide Residues in Food

- The available data indicate that fungicides applied in the production of food seldom result in detectable residues in food. When fungicide residues are found in food, they are usually orders of magnitude less than the allowable tolerances.
- Federal and state agencies that monitor the nation's food supply are aware of which pesticides are registered for each crop, which are recommended in each area, which are purchased and used in

various areas, how and when these are used on a particular crop, which disappear rapidly, which persist, and most importantly, which to look for.

- Selective surveys are used in addition to routine monitoring to determine the occurrence of a pesticide or chemically related pesticides in a number of different crops or they may focus on sampling a specific crop for one or more pesticides. If required, monitoring programs will focus efforts to analyze for pesticides associated with known or suspected health concerns.

- The fact that residues above tolerance are seldom found indicates that pesticide chemicals are generally used according to label directions. Although violative residues can result from misuse, unusual weather conditions, or poor agricultural practices, the most common cause is use of a particular pesticide on a commodity for which no residue level has been established (i.e. the pesticide is not registered for that use).

- Monitoring and Market Basket Survey data show an infrequent appearance and low levels of fungicide residues indicating dietary intake is well below the safety levels that have been established.

- As a rule residues are reduced further by processing. This has been the case illustrated for a number of fungicides. However, there are some cases in which processing leads to the accumulation of conversion products. The best known fungicide example of this is the conversion of ethylenebisdithiocarbamates (EBDCs) to ethylenethiourea (ETU). Procedures have been introduced in processing as well as crop production to reduce possibilities of ETU formation.

- A study on EPA's methods for setting tolerances for pesticide residues in food was conducted through the National Research Council (NRC). Risks were calculated for all pesticides considered oncogenic for which cancer potency factors were available. These calculations were based on the assumptions that (1) all residues were present at tolerance levels, (2) the majority of pesticides registered for use on a crop were used on that crop, and (3) 100% of the acreage of that crop was treated. This extremely exaggerated residue level scenario resulted in projections of very high cancer risk levels. Another study, using a specific crop as an example, indicated that when actual residue and incidence data were used for these calculations the risk was approximately 2500 times less. The NRC risk values could best be described as the theoretical maximum risk,

but because the exposure assumptions relating to frequency of use and level of residues were so deliberately exaggerated, the results have no relation whatsoever to actual risks.

- In considering the significance of fungicide (or other pesticide) residues in food, the basic elements of risk assessment must be understood. There is usually a level of exposure to any chemical which does not cause injury. Pointing with alarm to the presence of a chemical without reference to the level of exposure is entirely without merit and creates a perception that there is risk when, in fact, a risk analysis has not been presented.

CHAPTER 5 –
Exposure of Agricultural Workers to Fungicides

- In most instances, the health effects reported due to exposure to pesticides are acute effects. Since fungicides have a low mammalian toxicity, they are rarely the cause of acute intoxication; other classes of pesticides are more likely to be associated with these reported incidents.
- Proper working practices and protective gear are highly effective in substantially reducing both dermal and respiratory exposure to pesticides experienced by agricultural workers.
- The possibility of chronic effects from worker exposure to small amounts of fungicides or their residues over prolonged periods of time has sparked safety concerns. Unfortunately, in spite of the old adage, "the dose makes the poison", interest in chronic effects of fungicides has focused on the issue of cancer, raised by studies with laboratory animals exposed to unrealistically high doses of chemicals. Some evidence exists that chronic effects other than cancer may occur in humans. There are very few studies of the effects of long term exposure to low fungicide concentrations; such investigations would be worthwhile.

CHAPTER 1

OVERVIEW OF FUNGICIDES

I. INTRODUCTION

Fungi cause a variety of diseases in plants and animals. Under the right conditions some fungi can invade a healthy crop and destroy it completely within a few days or weeks. Of the 100,000 described species of fungi in the world, approximately 20,000 produce one or more diseases in various plants. Among these are 4,600 rusts, 700 smuts, 1,000 powdery and downy mildews. Fungi cause about three-fourths of all infectious plant diseases, and all economically important plants are subject to attack by one or more fungal species. Often 10 to 50 different fungi may cause disease of one plant species. Infection by fungi can cause great reduction in yield and product quality.

One of the most historically significant and best documented impacts of a fungal disease on a country is that of the potato late blight disease caused by *Phytophthora infestans*. Successive unchecked epidemics of late blight in 1845 and 1846 caused Ireland to lose over a quarter of its population: one million died from starvation and 1.5 million emigrated. Late blight occurs in cool, moist regions wherever potatoes are grown. During World War I late blight damage to the potato crop in Germany may have helped to end the war (Shurtleff and Kelmann, 1986). The cause of the potato late blight disease was not known at the time of the Irish late blight famine, and although it is now well understood, the

threat of epidemics still persists. Today, only the use of fungicides prevents massive losses from late blight when weather conditions are favorable for disease development.

Another fungal invasion that affected a whole nation was coffee leaf rust, caused by *Hemileia vastatrix*, which devastated coffee plantations of Ceylon (now Sri Lanka) in the late 1860's. Within fifteen years, losses due to rust were so crippling that coffee was abandoned completely and replaced with tea. These events are said to account for the status of tea as the national beverage of the British people (Bent, 1969).

Tea is susceptible to 380 fungal pathogens. In northeast India, where 190 fungi and 125 other pests have been detected, losses are estimated to be around 30 million kg (67 million pounds) of tea per year.

An estimated 60% of the total hard red spring wheat crop in Minnesota and the Dakotas was lost to black stem rust *(Puccinia graminis)* in 1935. In 1934 and 1935 the disease reduced yields of durum wheat by as much as 80% and of spring wheats by 30%. Losses were measured in the millions of bushels (Shurtleff and Kelman, 1986).

More recently the southern corn leaf blight epidemic of 1970 destroyed 15% of the U.S. corn crop, which was a loss amounting to 20 million metric tons of grain worth 1 billion dollars. Most of the corn planted in the U.S. at that time was susceptible to this new disease. Fortunately resistant varieties were available and were introduced quickly. Otherwise, even more destructive epidemics would probably have occurred in years subsequent to 1970.

Besides dramatic invasions, there are of course many region-specific fungal diseases which have the potential to damage farmers' crops year after year. Sheath blight, a devastating disease of rice, can only be poorly controlled in Arkansas with available measures. In 1984, 23% of Arkansas' rice yield was lost to the disease (Waldrum, 1985). There are also about 18 preharvest and 9 postharvest fungal diseases that afflict some 2.6 million tons of stone fruits in the U.S. each year. Estimated losses due to fungal-induced crop damage amount to about 20 percent of the world's agricultural production (Bent, 1979). Crop losses in the absence of fungicide use would increase dramatically.

In order to avoid famine or severe food shortages it is necessary to have fungicides or other means available to control plant diseases. There are a variety of non-pesticidal measures, such as using immune or highly resistant plant varieties, crop rotation, pruning and burning diseased parts, managing irrigation timing and drainage methods, modifying post-harvest handling techniques and storage conditions, and enforcing strict

quarantine regulations to control plant and seed importation into specific regions that reduce chances for disease occurrence. These basic farming practices combined with ecological principles, and the use of biological and selected chemical pest control methods form the basis of integrated pest management (IPM) which has been practiced over many years for the control of plant disease.

For the near term, there are no apparent new plant diseases control strategies that depart from those currently in practice. Biocontrols of fungal diseases utilizing microorganisms have been strongly promoted as possible substitutes for fungicides in recent years. The foundation of biocontrol is usually based on antibiosis, direct parasitism, nutrient competition or induced host resistance. Aside from the fact that most biocontrols are difficult to establish and unreliable in their effectiveness, they often involve the production of antifungal chemicals (antifungal antibiotics, metal binding chemicals, enzymes) for which safety has not been determined.

Fungicides are seldom used when a resistant variety is available or if the disease can be controlled by a cultural practice or other non-chemical methods. However, fungicide application is an integral part of most successful IPM programs and is absolutely essential for controlling many storage rots, seedling diseases, root rots, leaf blights, trunk cankers, rusts, smuts, or mildews, that can break through non-chemical defenses. The need for fungicides in plant protection is analogous to the need for antibiotics in human medicine. Without fungicides there would be devastating crop failures, higher food prices and a striking increase of fungal contaminated food. The ability to export food from local production areas to domestic and international markets would be severely curtailed.

II. HISTORY OF FUNGICIDES

The first use of a fungicide has gone unrecorded. Although the Old Testament contains many references to blights, blasts, mildews, rusts, and smuts, there seems to have been little or no effort to control them; such tribulations were accepted as an expression of God's wrath (McCallan, 1967). From the earliest times until well into the 18th century there are many references to the use of strange concoctions to control insects and what we now know as fungal diseases. Common ingredients were dung and urine of farm animals and occasionally lime or ashes, using the rational that insects dislike offensive tastes and odors (Hough & Mason, 1951). These unusual remedies and groping in the dark for others are to be expected since fungi were not clearly established

as a cause of plant diseases until Prevost's classic studies of smut in 1807 (McCallan, 1967). Historically, the development or use of fungicides can be divided into three periods: inorganic, organic surface protectants, and organic systemics.

A. *Inorganic Fungicides*

1. *Sulfur*. Sulfur in many forms is the oldest effective fungicide known; it is still in use today. The earliest references to the use of sulfur as an antifungal (or purifying) agent are found in Homer's "Iliad" and "Odyssey," two epic poems written in the eighth century B.C. describing Greek legends and customs of several centuries earlier.

The next record we have is from the Greek physician, Dioscardes, who advocated the dermatological use of sulfur ointments during the first century A.D. At about the same time, Pliny the Elder in his "Natural History," a collection of Greek folklore, recommended steeping seed grain in wine or in a mixture of bruised cypress leaves in order to control "mildew," which presumably was smut (McCallan, 1967).

Although sulfur has a long history of use, it was not until the early 1800's that lime sulfur was used agriculturally to control mildew on fruit trees. It is probable that many of the better informed gardeners were using sulfur at least by 1800, if not earlier. Credit goes to William Forsyth, "Gardener to His Majesty, &c. &c.," for his 1802 treatise on the use of sulfur in the culture and management of fruit trees (McCallan, 1956). A few years later the use of sulfur was extended to controlling powdery mildew on grapes.

2. *Copper*. Beginning in 1761 copper sulfate was used to treat wheat seed (Metcalf, 1971). In the Bordeaux (Medoc) region of France around 1886, Pierre Millardet discovered that a blue paint-like mixture of copper sulfate and hydrated lime, which farmers had long daubed on grapes growing along the roadside to help prevent pilfering, provided spectacular control of downy mildew, a very serious disease of grapes. McNew (1959) writes that Millardet saved the grape industry of France and "gave mankind a material that was to grow in importance and become the front-line defense against the ravages of fungi for the next seventy-five years."

One of the truly remarkable uses of this copper fungicide was the establishment of a vast pumping station and pipeline system of the United Fruit Company in Honduras in the 1930's, which supplied millions of gallons of Bordeaux mixture to the banana plantations to control Sigatoka. This severe leaf disease threatens banana-producing areas to such an extent that bananas cannot be produced without fungicidal sprays (Zentmyer, 1971).

Since the 1930's a number of fixed copper fungicides have been used. The practice of spraying copper fungicides in Kenya, for example, was prompted by the increase in fungal diseases; thus, most coffee farmers have found themselves committed to near monthly sprays of copper fungicides, especially under conditions of high rainfall (Aduayi, 1976). The bulk of the 8.3 million pounds of simple copper salts used annually in the U.S. is applied as fungicides on oranges and tomatoes (Anon., 1988).

B. Organic Fungicides

1. *Surface Protectant*. Many synthetic sulfur and other organic fungicides have been introduced over the past few decades to replace the more harsh, less selective inorganic materials mentioned above. The first of the organic sulfur fungicides, thiram, was developed in 1934. It is a member of the dialkyldithiocarbamate group originally developed as vulcanization agents for use in the rubber industry (Cremlyn, 1977). The ethylenebisdithiocarbamate, zineb, and the phthalimide, captan, were developed in the 1940's or early 1950's.

Organic fungicides such as the ethylenebisdithiocarbamates, known also as EBDCs (e.g., zineb, maneb and mancozeb), dialkyldithiocarbamates (e.g., thiram, ziram and ferbam), phthalimides (e.g. captan), chlorothalonil and dichlone as well as the inorganic copper and sulfur mentioned earlier are all classified as broad spectrum surface-protectants. Surface protectants are not absorbed or translocated by the plant in amounts adequate to achieve internal therapy. They must be present as a film on the surface of a plant at or before appearance of the pathogen in order to prevent infection. They are thus suited for prophylactic use only. Their action can also cause damage to the plant, since there may be little margin of safety between phytotoxicity and fungitoxicity (Crowdy, 1972). These characteristics limit the possibility of successful disease control, and in some cases exclude it (Scheinpflug, 1986). These fungicides have experienced very few problems with fungal resistance and therefore remain extremely valuable for use in conjunction with the systemic fungicides in resistance management programs designed to prevent or delay resistance to these highly specific systemic compounds.

2. *Systemic Fungicides*. In contrast to surface-protectant fungicides, systemic fungicides are absorbed by a plant and translocated within. Being internally therapeutic, they can cure plant diseases several days after infection has occurred. In other words, they may act curatively or eradicatively, a key advantage in many crop/disease situations. Because of their systemic properties and their eradicative effect, these fungicides are especially suitable for integrated pest management (Scheinpflug,

1986). Moreover, their activity is not affected by some of the environmental limitations that reduce the field effectiveness of surface-protectant fungicides (Barnes, 1977). However, these fungicides have experienced problems with fungal resistance which is in contrast to the less specific surface protectants.

A compound must satisfy several requirements in order to be a successful systemic fungicide. Since water is the carrier normally used during spraying, it must be deliverable in a soluble or suspended state. It must be able to penetrate the plant's natural barriers, including the waxy cuticle covering the leaf, the cell wall and the cell membrane. It must be stable against the plant's metabolism so the toxic moiety is not broken down before it has a chance to encounter the pathogen. Finally, the fungicide must be selective so it is toxic to the fungal pathogen, not to the plant itself (Edgington, 1981).

One of the first groups of compounds to demonstrate systemic activity in plants was the benzimidazoles. Thiabendazole was first described as having fungicidal activity in 1964. It had been previously used as an anthelminthic agent and is still used in treating roundworm and hookworm. Benomyl, another benzimidazole, was one of the first systemic agents to be used widely in plant disease control beginning in the early 1970's. The benzimidazoles are effective against all major groups of fungi, excluding the Oomycetes and Zygomycetes, and thus control a broad range of important crop diseases (Somerville, 1986).

The carboxamides (e.g., carboxin and oxycarboxin) are a group of fungicides that also came into practical use around 1970 (Buchenauer, 1975). They are highly systemic and possess selective action, principally against smut fungi, rust fungi and the soil fungus *Rhizoctonia solani* (Buchenauer, 1975).

Since the mid-1970's, a major impact on disease control has been made by systemic chemicals which inhibit sterol biosynthesis (Ragsdale & Sisler, 1972; Siegel, 1981; Kato, 1985; and Berg, 1986). These are the largest group of systemic fungicides with the same specific mode of action, and yet are a diverse group of compounds with respect to chemical structures (Siegel, 1981). Imazalil, triadimefon, fenarimol and triforine are examples from this group. In general, they show good systemic activity in plants, possess curative as well as preventive activity, and control a broad range of fungal diseases at relatively low dosages without phytotoxicity (Kato, 1985).

The systemic phosphonate fungicide fosetyl-Al appeared in the late 1970's. Fosetyl-Al is the only commercially available fungicide known to be systemically transported in a downward direction in plants,

permitting the fungicide to be applied to foliage or tree trunks in order to control root diseases (Fenn and Coffey, 1987). The fungitoxic mechanism of fosetyl-Al is unknown. Disease control may involve a fungitoxic action that is assisted by an increase of host-plant resistance (Sisler and Ragsdale, 1987).

Other important fungicide groups introduced into practical use since 1970 include the phenylamides (metalaxyl, furalaxyl, benalaxyl, ofurace, cyprofuram and oxadixyl) which are specific for Oomycetes (Schwinn & Stub, 1987; Davidse, 1987) and the dicarboximides iprodione, procymidone and vinclozolin (Pommer & Lorenz, 1987) which are used to control *Botrytis* and several other pathogens. The fungicide cymoxanil, which is used to control diseases caused by Oomycetes, has also been introduced since 1970 (Schwinn & Staub, 1987).

A further step toward selective action is the development of non-fungicidal compounds which interfere with the disease process without being directly toxic to fungal pathogen. Such chemicals might act by increasing the resistance of the host plant or decreasing the virulence of the parasite. Tricyclazole, which interferes with fungal penetration of plant cell walls, is an example of such a compound. In addition to a highly selective action, these chemicals could also have other advantages, such as a longer lasting overall protection of the plant resulting from an induced resistance and a reduced chance for the development of fungicidal resistance (Dekker, 1986). There are good prospects that chemical regulation of host resistance or of fungal pathogenicity by non-fungicidal compounds will increase in significance as mechanisms of disease control are better understood. Progress in this area is presently hindered by a lack of fundamental knowledge of fungal pathogenicity and host/parasite interactions which lead to resistance or susceptibility (Sisler & Ragsdale, 1987).

III. MODE OF ACTION AND SELECTIVITY

During the development of a new fungicide, a variety of experimental results are required to determine its mode of action. After investigating the level of activity, the antifungal spectrum (i.e., the number of fungal species for which it is effective), and the influences of pH and composition of the medium on activity, respiratory inhibition must be determined and whether certain compounds (growth factors, amino acids, -SH compounds) can act as antagonists of the fungitoxic agent. Also, primary and secondary effects must be distinguished. For instance, cell rupture leads inevitably to respiration inhibition; alternatively, inhibition of energy production results in a decrease of biosynthesis.

Also, a determination is made whether the agent exerts a fungistatic or fungicidal effect. The structure of an antifungal agent can sometimes give a clue to its mode of action. There is also a question of whether the fungicide is itself the actual toxic agent or whether the true toxicant is only formed in the medium or by metabolic activity of the fungus. Only from a careful analysis of such data can a hypothesis on the biochemical mechanism of action be derived and validated (Kaars Sijpesteijn, 1972).

Many of the inorganic fungicides (e.g., sulfur) and other organic multisite inhibitors (e.g., EBDCs) interfere with energy production (Sisler and Ragsdale, 1985). The systemic fungicide carboxin also interferes with this process by blocking a specific site in the electron transport pathway (Mathre, 1971). Other systemic fungicides interfere with many of the biosynthetic processes that are necessary for production of new cell material required for growth, maintenance and virulence of the fungal organism. Inhibition of biosynthesis sometimes has only a fungistatic effect, i.e., halting fungal growth without a lethal effect.

Benomyl and other benzimidazole fungicides interfere with the cell division process by binding to the beta tubulin subunit in sensitive organisms and blocking mitosis (Sisler and Ragsdale, 1985). Benomyl's fungicidal activity is thought to be derived from its hydrolysis product, carbendazim (Clemons & Sisler, 1969). Reports from benomyl degradation studies (Chiba & Veres, 1981) have shown benomyl dissipated quickly on McIntosh and Red Delicious apples and that carbendazim concentration gradually increased after repeated applications of benomyl. Cline & Neely (1981) suggested that gradual loss of effectiveness is due to the ultraviolet photodecomposition of carbendazim.

Inhibition in the sterol biosynthetic pathway is the mode of action of a large group of chemically diverse compounds including imazalil, fenarimol, triadimefon, propiconazole and triforine. Certain sterols are important in membrane structure and function. Abnormalities are noted in the morphology of cell walls and membranes in fungal cells exposed to these compounds. Ultimately a modification of the membrane structure can result in detrimental or lethal effects to the cell (Sisler and Ragsdale, 1984).

Ribosomal RNA synthesis in the group of fungi known as the Oomycetes (includes the potato late blight organism, *Phytophthora*) is the inhibition target of the phenylamide fungicides (e.g., metalaxyl, oxadixyl and furalaxyl) (Davidse, 1987).

The antibiotic cycloheximide is an example of a fungicide that acts primarily by blocking protein synthesis. Cycloheximide inhibits this process by interfering at the ribosomal level (Siegel, 1977).

In order to establish an infection in plants, fungi must often penetrate the cutanized epidermal walls of plant cells. This penetration process involves special enzymic activity, mechanical force or a combination of both. The fungicides that inhibit biosynthesis of the pigment melanin block the capacity of the rice blast pathogen to penetrate cutanized plant epidermal walls. The best known of these compounds, which are used to control rice blast disease, is tricyclazole. Melanin or an oxidized melanin precursor appears to give the fungal wall the rigidity needed to penetrate the plant wall; without these penetration and subsequent infection do not occur (Sisler and Ragsdale, 1985).

The mode of action of some fungicides remains unclear. The dicarboximides (e.g., vinclozolin, iprodione and procymidone) appear similar in their primary effects to aromatic hydrocarbon fungicides such as chloroneb, quintozene and dicloran. Although membrane damage, interference with nuclear function and interference with cellular motile functions have been suggested, it remains unclear whether these are primary or secondary effects. These compounds may react with cellular enzyme systems to produce oxygen radicals. These in turn could produce the aforementioned effects (Lyr, 1987). The exact mechanism of action of these compounds has not been satisfactorily resolved.

The phenomenon of fungicide selectivity is very complex and knowledge of the biological processes involved is still scanty. Further advances in the chemical control of fungal diseases will depend to a large degree on a better understanding of the factors which control the selective action of a compound. From a theoretical point of view and from experimental data, it can be deduced that one or more of the following possibilities account for the differences in sensitivity of various fungi to a fungicide (Lyr, 1987)

1) Differences in the structure of the receptor or target system.
2) Differences in the accumulation of a fungicide in the cell.
3) Differences in the ability to toxify (activate) a compound.
4) Differences in the ability to detoxify a compound.
5) Difference in the degrees of importance of a receptor or target system.

IV. USE OF FUNGICIDES

To employ a fungicide successfully, the toxicant must be present at the correct time and in a sufficient quantity to be lethal to the fungus. Some disease control programs require repeated applications of chemicals. Timing, persistence, stability and redistribution are only a few of the parameters which influence effectiveness in the field (Barnes, 1977).

Fungicides are applied to a variety of sites and in a variety of ways:

1) To seeds to prevent infection by fungi which inhibit germination (Lewis, 1988).

2) To soil as fumigants to reduce the population of harmful fungi before seeds are planted.

3) To soil as prevention of disease (Van Wambeke et al., 1980).

4) To established plants as post-planting treatments to control root diseases. To fruit or foliage as a preventative spray.

6) Internally to plants, to eradicate or prevent infections of stems or leaves (Zentmyer, 1971). Dutch elm disease, for instance has been controlled by injection of carbendazim into tree trunks.

7) Postharvest to fruit and vegetables to increase shelf life. For protection against post-harvest diseases some fruit are also dipped into suspensions (Watkins, 1976). As a postharvest treatment of citrus fruit, metalaxyl was effective when incorporated into a wax coating for in vivo control of brown rot caused by *Phytophthora citrophthora*.

Farmers do not use all approved fungicides available for use. Appendix A lists 137 fungicides from the Pesticide Chemical News Guide (Duggan et al., 1988) and the Farm Chemicals Handbook (1988). The U.S. Government Code of Federal Regulations lists about one hundred fungicides registered for use. Among these, a few make up the bulk of fungicidal use on agricultural commodities. Sulfur leads in fungicidal poundage. According to the Sulfur Institute, the use of sulfur has increased by more than 150% over the past decade (Anon., 1989).

An example of fungicide use can be found in The Pesticide Use Report issued by the State of California's Department of Food and Agriculture which provides a partial list of the amounts of fungicides used in California. The quantities listed include only those applied by professional applicators or materials designated as restricted in California. In California, the leading agricultural state in the nation in terms of farm gate value, 25.6 million pounds of sulfur were applied to control mites and fungi in 1987, out of a total of almost 94 million pounds of agriculturally relevant pesticides (CDFA, 1989). Sugar beets,

grapes, and tomatoes each accounted for more than ten percent of sulfur's total use. Other major fungicides include various copper compounds, captan, chlorothalonil, dicloran, sodium arsenite, benomyl, the EDBCs and the dialkyldithiocarbamates. They are used on a large variety of crops. Table 1.1 lists the top-ten fungicides used in California, in decreasing order of overall pounds used, and the high use crops on which they were applied in 1986 (i.e., on which their use comprised more than ten percent of their total reported use in California).

TABLE 1.1

TOP-TEN FUNGICIDES AND THE HIGH USE CROPS ON WHICH THEY ARE USED IN CALIFORNIA, 1986

Crops	*Lbs.*	*Acres*	*Avg. Lbs./Acre*
SULFUR:			
sugar beets	8,114,514	235,308	34.5
grapes	6,457,638	582,332	11.1
tomatoes	2,917,906	123,855	23.6
COPPER SALTS:			
walnuts	288,653	50,044	5.8
almonds	266,392	73,286	3.6
oranges	218,217	260,977	0.8
ZIRAM:			
almonds	879,831	164,566	5.4
MANEB:			
lettuce (head)	441,040	196,911	2.2
CAPTAN:			
grapes	200,050	85,704	2.3
almonds	83,329	27,992	3.0
prunes	65,003	17,728	3.7
strawberries	55,469	35,115	1.6
CHLOROTHALONIL:			
tomatoes	110,858	55,927	2.0
celery	53,988	37,431	1.4
MANCOZEB:			
potatoes	75,158	55,678	1.4
tomatoes	52,624	27,820	1.9
onions	41,989	40,213	1.0
DICLORAN:			
lettuce (head)	60,158	21,799	2.8
grapes	26,812	18,508	1.5
celery	21,356	6,340	3.4
lettuce (leaf)	19,466	7,595	2.6
BENOMYL:			
almonds	40,052	55,702	0.7
grapes	11,807	18,541	0.6
strawberries	11,771	26,668	0.4
SODIUM ARSENITE:			
grapes	43,936	6,670	6.6

Source: CDFA, 1987a.

Although there are some commodities on which only one fungicide is registered for use (such as copper oxide on artichokes and metalaxyl on lentils), several fungicides are registered for use on most agricultural commodities (e.g., 36 are registered for use on apples and 37 for use on peaches). However, a grower may use none or only a few of these per season. A particular fungicide may be used to control various diseases on a variety of crop plants. For example, benomyl is used for control of 60 diseases, chlorothalonil for 81 and zineb for 58 (Page and Thompson, 1986).

The California Tomato Growers Association surveyed growers of processing-bound tomatoes in order to determine which pesticides were used during the 1986 growing season. These farmers reported using herbicides, insecticides, soil fumigants and growth regulators. Although tolerances existed for the legal application of 20 fungicides, no farmer used all of them (see Table 1.2). Considering that these products compete with each other for many uses, such data prove a logical intuitive conclusion: just because a pesticide product is registered does not mean that it is always used. Just as people do not buy every brand and type of household cleaner or laundry detergent available for use in the home, farmers do not purchase or use every available agricultural chemical (TAS, 1987).

TABLE 1.2

PERCENTAGE OF CALIFORNIA TOMATO FARMERS USING PESTICIDES, 1986

Pesticide Class	*% Farmers Using*						*Maximum*	*No.*
	0	*1*	*2*	*3*	*4*	*5 **	*No. Used*	*Registered*
Fungicides	23	48	26	3	0	0	3	20
Growth regulators	85	15	0	0	0	0	1	3
Herbicides	35	19	33	19	4	0	4	7
Insecticides	31	26	26	12	4	1	5	54
Soil fumigants	76	22	2	0	0	0	2	4

*Indicates number of different pesticides used.

Source: TAS, 1987.

These data represent the typical situation in agriculture. Need and cost, rather than availability, dictate the use of pesticides. A farmer is not likely to use a particular pesticide unless the benefits (e.g., prevention of crop loss, destruction of pests producing a health hazard, improved quality and aid in harvesting) exceed the costs of applying it. Different parts of the country have different weather conditions and pests and,

thus, different pesticide needs. Also, many products compete with each other, so cost and effectiveness are factors determining which pesticides are used. For example, mebenil is effective as a foliar application against rust fungi, such as *Puccinia striiformis* on barley and wheat and P. *hordei* on barley. However, the iodine derivative, benodanil, proves to be more active than mebenil in controlling cereal rust diseases and appears to be better tolerated by plants. Other carboxylic acid anilide fungicides are more active against smut and rust diseases following seed or soil treatment than others, but inferior for foliar treatment (Buchenauer, 1975). Application rates necessary for pest/disease control may be lower than maximum rates advised on the label or allowed by law; therefore, less pesticides will be used.

V. *FACTORS AFFECTING EFFICACY*

It is important to consider the effect of the environment on a fungicide. The scientific literature is replete with structure-activity data from which predictions of practical performance of a fungicide might be made. However, one problem that has plagued researchers is the failure of fungicides in the field that had seemed promising in the laboratory. A number of factors impact the effectiveness of a fungicide including its physical form and any physical action or biological activity to which it is subjected (Rich, 1960).

A number of studies have demonstrated the relationship between particle size and both fungitoxicity and tenaciousness on the plant. Bordeaux mixture, for instance, can be made more effective by formulation with certain wetting agents, and copper oxide succeeded as a foliar fungicide only after each particle was first coated with gum arabic. Very often fungicidal candidates fail in practice because they were not subjected to the extremes of weathering that exist in nature, such as wind whipping of leaves, leaf expansion, sunlight, long periods of continuous high humidity with attendant carbonation and oxidation, and periodic wetting and drying which tends to increase hydrolyis. Finally, there are the effects of biological activity; compounds may be degraded either by plant metabolic processes or by soil microorganisms. Such degradation can, in certain cases, even increase fungitoxicity. On the other hand, a loss of fungicidal efficacy following repeated soil applications may result from an increase of microorganisms that use the fungicide as a substrate. This phenomenon is referred to as enhanced biodegradation (Kaufman et al., 1985).

Resistance of pathogens to fungicides is understandably a major concern. Although resistance problems with insecticides and antibiotics have

been known for several decades, it has only been since the introduction of the highly specific systemic fungicides that fungicide resistance has been a problem. The sudden appearance of resistance in a pathogen population may result in failure of disease control and, consequently, serious crop losses, when it is not recognized at an early stage (Dekker, 1982). The extent to which it is a problem to farmers depends upon the characteristics of resistant mutants, the biology of the pathogen, and the intensity of use of a particular chemical on one commodity causing an extreme selection pressure on a pathogen. For example, the intensity of benzimidazole use, coupled with its specific mode of action, has led to the severe problem of resistance from some 23 fungal genera (Somerville, 1986). In view of the possible widespread and intensive use of sterol biosynthesis inhibiting fungicides on apples, Jones (1981) stressed the need to discuss use strategies to limit the possibility of a fungicide-resistance problem. One proposal is to formulate them in mixtures with unrelated fungicides or to restrict their use to certain parts of the growing season to reduce selection pressure on pathogens. Had such a strategy been followed when benomyl was first introduced, resistance to this fungicide would perhaps be less of a problem than it is today.

Preventing or delaying resistance may require that fungicides be rotated so that, periodically, chemicals with different modes of action will be employed. An alternate approach, referred to above, involves applying mixtures of chemicals with differing modes of action. In either case, it is necessary that a variety of fungicides be available (i.e. registered) for each commodity. This is a troublesome point for today's growers, who worry that the dwindling arsenal of registered fungicides still available may lead to overuse of specific chemicals thus hastening resistance problems. The older surface-protectant fungicides such as captan, maneb, chlorothalonil and thiram are vital for resistance management programs designed to prevent or delay fungal resistance to the newer systemic fungicides and as alternatives if the latter lose effectiveness because of resistance. The success of resistance-preventing strategies will depend to a great extent on educating individual growers.

The socioeconomic impact of the resistance phenomenon affects the farmer, consumer, manufacturer, pest control advisor, national regulatory authorities, and the ancillary agrochemical industry (including packers, shippers and on to the entire community). Crop losses hurt farmers and consumers. Fungicide resistance confronts not only manufacturers with a potential for product liability, but also pest control advisors who must determine how to control a pathogen. Regulatory authorities should understand that canceling the use of older surface-protectant fungicides that are not subject to pathogen resistance

will almost certainly result in much more serious fungal resistance problems for systemic fungicides. Systemic compounds are highly desirable for many reasons including the smaller quantities required for successful disease reduction as well as the opportunity to delay application until a disease situation arises; however, resistance management programs are essential for their successful use. Finally, the agrochemical industry has the potential to lose a large investment in a fungicide if its use leads to resistance problems. Thus, it may be hesitant to develop new pesticides in the future (Schwinn, 1982).

VI. SUMMARY

Fungicides play a critical role in integrated pest management approaches to disease control. They are seldom used when a resistant crop variety is available or if the disease can be controlled by non-chemical methods such as cultural practice. Many crops, however, require some degree of chemical control for fungal diseases which can cause great reductions in yield and product quality. Without fungicides there would be devastating crop failures, higher food prices, adverse community economic impacts and a striking increase of fungal contaminated food. The ability to export food from local production areas to domestic and international markets would be severely curtailed.

Fungicides are effective through a variety of mechanisms such as interference with energy production, various biosynthetic processes or cell structure. It has only been since the introduction of the highly specific systemic fungicides that fungicide resistance has been a problem. The older surface-protectant fungicides such as captan, maneb and chlorothalonil, which are multi-site inhibitors, are critical in resistance management programs designed to prevent or delay resistance to the newer systemic fungicides and as alternatives if the latter lose effectiveness due to resistance.

CHAPTER 2

ADVANTAGES TO THE PUBLIC FROM THE USE OF FUNGICIDES IN AGRICULTURE

I. INTRODUCTION

Important advantages result from use of fungicides. The perception of these vary with the farmer, the pesticide manufacturer, and the citizen or elected representative (Machemer, 1986). Advantages for the farmer are the prevention of yield losses, achievement of improved crop quality to enhance market opportunities, facilitation of farmwork and harvest, and improvement of the cost/profit ratio. The advantage for the citizen is an ample, varied, safe, healthy and inexpensive food supply available throughout the year. The importance of adequate dietary levels of fruits, vegetables and carbohydrates for reducing chronic disease risks, especially for heart disease and cancer, has been strongly emphasized by the Committees on Diet and Health of the Food and Nutrition Board, Commission on Life Sciences of the National Research Council (NAS, 1989). The dietary trends in the future will almost certainly be toward lower meat and animal fat consumption and toward higher consumption of fruits, vegetables and cereals. Not only will fungicides be needed to sustain production of these commodities, but also to prevent their

contamination with fungal toxins (mycotoxins) and toxic plant defense chemicals (phytoalexins) produced by plant tissue in response to fungal infection.

With the high quality of food products available at present to the American public, little thought is given to these naturally produced toxins. However, there is an awareness by food and medical experts that problems already exist in the Inter-American Region. The Inter-American Conference on Food Protection of the National Research Council has ranked (a) microbiological hazards and (b) natural toxins and environmental contaminates of food as greater risks than improper use of pesticides (NAS, 1987a, Food Protection in the Americas). The role that fungicides play in preventing food contamination with toxic fungal products and plant defense chemicals in fungal infected plant tissues is not widely recognized. While legislation exists to evaluate risks associated with the use of fungicides (and to regulate their use) there are currently no mechanisms established to balance these risks against risks from toxic natural products that will surely increase if fungicides are not used. Responsible regulation of fungicide uses, therefore, calls for balancing the risks.

Banning the use of a fungicide causing a very small risk may expose the public to fungal food contamination presenting much greater risks due to mycotoxins and fungal induced phytoalexins. In view of the fact that we have information on the toxicological hazards of only a few of the hundreds of agriculturally significant fungi, the safest course to follow would be to prevent fungal infection or contaminations of food products whenever possible.

II. AVAILABILITY OF AGRICULTURAL PRODUCTS

Fungal diseases can have immediate, devastating effects on crops, on communities, a state's economic health, and on the public's health. For example, sudden-death syndrome (SDS) of soybeans is a mysterious disease that was first observed in 1970. Although SDS was first thought to be caused by nutrient deficiency and herbicide carry-over, evidence now points to a new strain of *Fusarium solani*, form A, which is a soil-borne fungus. Arkansas had 30,000 to 60,000 acres affected in 1984 with losses of 20–70%, worth $3 million. The disease hit its peak in Kentucky in 1985: 50,000–60,000 acres had significant levels of SDS with yield reductions of 20–60% or more. The disease also is favored by cool, wet weather. This means that in years of adequate precipitation, when farmers normally count on yields to make up for previous dry years, SDS can cause devastating crop and economic losses. Preliminary research on

in-furrow fungicides and methyl bromide-chloropicrin fumigation for SDS control is currently underway (Brosten & Simmonds, 1989).

Interest in foliar fungicides to control diseases in wheat has increased in recent years, because of expanded wheat acreage in specific areas of the country where increased incidence of foliar diseases results in associated yield losses. Among the major foliar diseases of wheat are glume blotch, which has caused up to 55% yield losses in Illinois wheat; powdery mildew; and leaf rust, which may be the most widely distributed wheat disease known. Foliar fungicide applications are worthwhile when pressure from diseases is high enough to cause significant yield losses. One study from 1978 to 1982 in Tennessee showed that treatments each year provided an average yield increase of 16 bushels per acre, or a 28.3% increase, together with "excellent control of all foliar diseases" (anon., 1985).

In Oklahoma, commercial production of asparagus increased from 60 ha in 1981 to more than 200 ha in 1984. Asparagus is a perennial crop remaining productive for more than 15 years. The amount of yield depends on the age of the crowns and the amount of carbohydrate stored in the root system by the fern during the previous season. Thus, to have bountiful harvests, it is necessary to keep the plant healthy and the ferns free of *Cercospora* blight that would otherwise cause defoliation decreasing the following year's asparagus spear harvest. Again, fungicides play a vital role in warding off disease. One study, involving various mixtures of chlorothalonil and mancozeb, showed that fungicide treatments increased yields by 40.2 to 82.1% over controls (Conway et al., 1987).

Almond trees are subject to several flower, fruit, and foliage diseases. The most common of these is brown rot, which causes death of flowers and twigs; shot hole, which causes defoliation; and jacket rot, which destroys young fruit. All three diseases are favored by rainfall, so growers regularly use control measures in northern and central California orchards, where rainfall during bloom is expected in most years. Pest and disease control are important in California where 100% of the U.S. market of almonds is produced, worth $462 million in 1986 (CDFA, 1987c). Results of a seven-year study on the efficacy of several fungicides in controlling almond shot hole disease showed that captan, captafol (not currently registered for use on almonds), iprodione, maneb, and copper + ziram protected significantly against yield losses in 1986, a heavy-disease year. (In years when disease incidence was low, the choice of fungicide had little effect on control.) Increases in pounds of nutmeats per tree ranged in 1986 from 174 to 239% over controls (Teviotdale et al., 1989).

The use of sulfur dioxide to control *Botrytis cinerea* during table grape (*Vitis viniferas* L.) storage has been practiced for more than 50 years. A problem with this fumigation method is that the concentration of SO_2 required to control the disease is very close to the levels that can damage the fruit itself by bleaching berries and causing premature stem browning, both of which decrease grape marketability. Marois et al. (1986) showed that a reduced rate of SO_2 fumigation used at a shorter interval could increase disease control and decrease adverse effects.

Fungicides also control decay of other fruit in storage, such as prunes. Dehydration facilities being limited, growers must decide to either harvest their crop before maturity or store the fruit until dehydration is scheduled. The problem with the second alternative is that at least six genera of fungi are associated with fresh prune decay in storage. Such decay must be kept to a minimum. The predominant fungus is *Cladosporium herbarium*. Depending on the manner of harvest (mechanical or hand-picked) and (storage 20 or 28°C for four days), Michailides et al. (1987) determined that prune decay was as high as 95%. In general, mechanical harvesting was less damaging to prunes than hand harvesting, but treatment with the fungicide etaconazole allowed only 2% decay after 4 days at 20°C, which was a 94% reduction in decay compared to the controls.

These few examples illustrate the general importance of fungicidal controls. Without these controls there would be reduced yields of soybeans, wheat, asparagus, grapes, prunes and many other crops as a result of fungal disease damage. In addition to reduced yields, an increase in fungal infections or contaminations would lead to increased health hazards arising from mycotoxins and plant defense chemicals. These problems will be considered in the following sections of this chapter.

IMPROVED FOOD SAFETY

A. *Fungal-produced poisons (mycotoxins)*

Mycotoxins include fungal products which are carcinogens, nerve poisons, liver and kidney poisons or poisons of other organs. "Farmer's lung", for instance, is a condition associated with lung lesions and inflammations of the bronchi caused by respiratory exposure to moldy hay. Its acute symptoms were first described by Campbell (1932); its pathology was later reported by Seal et al. (1968). Mycotoxins can also produce birth defects, abortions, tremors, and cancers (CAST, 1979). Asthma from molds, spores, and dust is known as well. For example, Davies et al. (1988) described a type of occupational asthma in tomato growers following an outbreak of *Verticillium albo-atrum* in the crop.

Fungi produce mycotoxins in living plants, decaying plant material, and stored plant material. Three broad factors influence actual mold growth and mycotoxin formation (Hesseltine, 1976): (1) physical (moisture, temperature, mechanical damage, blending of grain, hot spots, time); (2) chemical (nature of substrate, mineral nutrition, chemical treatment, availability of carbon dioxide and oxygen); and (3) biological (plant stress, invertebrate vectors, fungal infection, plant varietal differences, fungal strain differences, spore load, and microbiological ecosystem).

Fungi that form mycotoxins occur worldwide. Foods can become contaminated with mycotoxins by fungi in the field, after harvest, in storage, or during processing of foods and feeds. Some mycotoxins, such as aflatoxins, occur in the field and can increase after harvest. Other mycotoxins, such as ergot toxins, are produced prior to harvest. Shipping grains, seeds and cereals from developed countries to developing countries normally involves long sea voyages of three to eight weeks between regions of different climates (hot to cold zones, dry to humid zones). Transit time can be extended further when ships are held up in ports for mechanical or political reasons (Bhat, 1988; Milton & Pawsey, 1988). These factors contribute to mold deterioration of agricultural commodities during transit with financial losses and health threats. The Food and Agriculture Organization of the United Nations has estimated that a quarter of the world's food crops are contaminated with mycotoxins (Mannon & Johnson, 1985). Tanaka et al. (1988) reported natural contamination of foods by *Fusarium* spp. toxins in 19 countries. Wheat, barley, oat, rye, corn, rice, and their products were positive for nivalenol, deoxynivalenol, and zearalenone in approximately half of the 500 samples taken. Some examples of food contamination with mycotoxins follow.

1. *Patulin and tenuazonic acid.* An example of a mycotoxin in fresh food resulting from fungal infection is patulin in apple. "Organic" apple juice contains varying amounts of patulin, a tumorigen in laboratory animals, which is produced by molds such as *Penicillium expansum* that infect apples, pears and cherries (Richardson, 1989). Contamination depends on the proportion of decayed apples used. Some "organic" apple cider is reported to contain up to 45 ppm of this mold metabolite (Richardson, 1989). Infections by this fungus can be controlled by postharvest treatments with fungicides.

Another example of mycotoxins found in fresh foods are the *Alternaria* toxins. *Alternaria* species are common plant pathogenic fungi that infect a wide variety of crops including apples, lemons, tomatoes and cherries. Grain crops, hay and silage are often contaminated with *Alternaria* as a field infection (Harvan and Pero, 1976). The toxicity of *Alternaria* is

well established. Among *Alternaria* isolates from a variety of food crops, 90% were lethal to rats when fed in a corn-rice mixture. *Alternaria* metabolites represent several structural classes of compounds including dibenzopyrones, anthraquinones, tetramic acids and polypeptides. The major mammalian toxin is believed to be tenuazonic acid (Harvan and Pero, 1976). *Alternaria* infected apples, tomatoes and lemons contain tenuazonic acid and several other mycotoxins (Stinson et al., 1981). These infections are normally controlled by fungicides. Lemons have often been treated postharvest with 2,4–dichlorophenoxyacetic acid to maintain tissue resistance to *Alternaria* infection (Eckert, 1977).

2. *Aflatoxins*. Of all the mycotoxins, aflatoxins are believed to be the greatest threat. Aflatoxins are the most potent carcinogens known. They are a group of structurally related toxic compounds produced by two fungal strains, *Aspergillus flavus* and A. *parasiticus*, which occur world-wide in many agricultural commodities. The name *aflatoxin* was formed from *a* for *Aspergillus* (the genus), *fla* for the species flavus, and the appended noun *toxin*, meaning poison. Fungal growth and aflatoxin production are favored by warm temperatures and high moisture typical of tropical and subtropical areas, including the southern United States. Commodities with the highest risk of aflatoxin contamination include corn, peanuts, cottonseed, and tree nuts (especially brazil and pistachio nuts); they are also found in animal products such as milk, milk products, and certain meat products of swine, where contaminated feeds have been ingested (CAST, 1979). As might be expected, significant losses from aflatoxin contamination are experienced by the peanut, corn, cottonseed, poultry, cattle and swine industries. Commodities with a slightly lower risk of aflatoxin contamination include almonds, pecans, walnuts, figs, raisins, and spices. Soybeans, beans, other pulses, cassava, grain sorghum, millet, wheat, oats, barley, and rice are resistant or only moderately susceptible to aflatoxin contamination in the field. Nonetheless, excessive amounts of aflatoxin can occur when any of these commodities are stored under high moisture conditions with insect or rodent infestations exacerbating the problem (CAST, 1989).

Aflatoxins produce both acute and delayed effects in humans. A disastrous acute poisoning occurred in a local area in India in 1974, when some 106 people died and 297 others became ill from eating corn heavily contaminated with aflatoxins (6.25 to 15.6 ppm) (CAST, 1979). Chronic hazards include hepatocellular carcinomas for people whose diet primarily contains contaminated commodities as peanut meal, cottonseed, and corn, or their products (Palmgren & Hayes, 1987).

In the U.S. such commodities are routinely tested for aflatoxin (and other mycotoxin) levels. The Food and Drug Administration (FDA) has set the action level for aflatoxins at 0.02 ppm. This is higher than that for some other countries: the Japanese government is considering a 0.01 ppm maximum limit on aflatoxin in U.S. corn purchases, and the Soviet Union has a maximum tolerance of 0.005 ppm aflatoxin in purchased corn (Brosten, 1989). In a six-year study (1977–1982) of preharvest corn in Georgia (U.S.) it was shown that the incidence of aflatoxin contamination ranged from 57% in 1982 to 100% in 1980. Insect damage contributed significantly to enhance the *Aspergillus flavus* population and subsequent aflatoxin contamination (McMillian et al., 1985).

A five-year study (1976–1980) of mycotoxins in Virginia wheat and corn found aflatoxin in one-quarter of the corn samples every year. The average levels in corn ranged from 0.021 to 0.137 ppm. Wheat samples, however contained no aflatoxins (Shotwell and Hesseltine, 1983). The National Peanut Council reported that peanuts are routinely tested for aflatoxin content and the mean toxin content is much less than the 0.02 ppm Federal action level in more than 95% of the lots (CAST, 1989).

Sorenson et al. (1981) suggested that measurements of aflatoxin in whole corn might underestimate actual levels in corn dust aerosols, which can be hazardous when inhaled. When components of a corn sample containing 130 ppb aflatoxin B_1 were analyzed, it was found that particles with diameters 7 to 11 μm had a aflatoxin content of 0.695 ppm, and two particles smaller than 7 μm had even higher levels of aflatoxins (1.175 and 1.814 ppm, respectively) than the sample as a whole. Because of the increased toxicity of respirable corn dust particles, it is important that their presence in corn be kept to a minimum.

Once grain is stored, moisture levels play a critical role in determining the extent to which aflatoxin contamination occurs. Infection poses serious problems in storage conditions with relative humidity of 75 to 90%. Stored sorghum with a moisture content of 15% became infected within a week even in the presence of large doses (290 to 310 ppm) of thiram. When stored with a moisture content of less than 15%, corn was free from infection for more than 90 days (Rangaswamy et al., 1971).

Chemical controls have been sought to protect crops from *A. flavus*. Propionic acid and sodium acetate seem to be useful for short-term storage of grains, provided they are added before any *A. flavus* growth has occurred. Aflatoxin levels in corn can increase by as much as 6% per hour in truckloads waiting to dump at grain dryers. The DuPont company considered having benomyl registered for control of aflatoxin

in stored corn and incorporating the fungicide with corn as it was augered into trucks or temporary storage bins. Although the treatment was effective, DuPont did not believe enough growers would be receptive to its use; there are few incentives (presumably financial) for marketing aflatoxin-free corn (Brosten, 1989).

Other companies, however, have tested fungicides for controlling mold in stored grain. ICI Americas has achieved positive results from A0523, a broad-spectrum fungicide with the same active ingredient as hexaconazole, which is registered in Europe for application to cucumbers, squash, and melons. When applied at 100 ppm to stored corn in Illinois, *A. glaucus* infestation of kernels dropped to 30%, compared to 55% in the controls.

Although *A. glaucus* does not produce aflatoxin, it is considered undesirable in stored grain, and its presence warrants additional testing for the more dangerous fungus. When 0A532 was applied at 80 ppm to corn samples, observed growth of all types of fungi was limited to 5% of kernels, compared to 48% of untreated kernels (Brosten, 1989).

Recent studies have shown that aflatoxin production in A. flavus cultures can be completely blocked by 8 ppm of clobenthiazone (Wheeler, et al., 1989). Even 1 ppm of this inhibitor blocked 75–90% of aflatoxin production while having little or no effect on fungal growth. Clobenthiazone is believed to block the aflatoxin biosynthetic pathway at a site prior to norsolorinic acid. Potent inhibitors of this type may prove to be very useful for preventing aflatoxin production in grains and other food commodities.

Because insect damage has been correlated with a high incidence of aflatoxin contamination, effective insect management should reduce the occurrence of aflatoxins in crops (Palmgren & Hayes, 1987). Insect vectors are culprits in fungal infection because they carry fungi internally and externally. Weevils are responsible for a high incidence of infection by *A. ochraceus*, *A. restrictus* and *A. flavus*: 25 to 100% in sorghum, 32 to 100% in wheat, and 20 to 94% in rice. These saprophytic fungi, which include some mycotoxin producers, are carried in the alimentary canal of the insect (Hesseltine, 1976).

3. *Fusarium toxins*. Mankind has suffered from the effects of Fusarium toxicoses throughout history. Trichothecenes are strongly implicated in such human maladies as alimentary toxic aleukia (ATA), stachybotryo–toxicosis and esophageal cancer. ATA results in decreased formation of red and white blood cells and platelets and led up to 60% of the mortalities in some parts of Russia in the first half of this century

(Shank, 1978). Zearalenone is of considerable concern because of its estrogenic activity. Moniliformin is a potent liver toxin.

Although contamination of foods and feeds by *Fusarium* is a well documented, worldwide phenomenon, the occurrence of these mycotoxins in foods for human consumption is less well known. *Fusarium* species are known to cause rots of fruit and potatoes and there is considerable concern about the possible effects of the diseased tissue on human health (Marasas et al., 1984). Data indicate that the four most important *Fusarium* mycotoxins, from a standpoint of human exposure, are deoxynivalenol (DON, vomitoxin), nivalenol, T–2 toxin, and zearalenone. These compounds frequently occur simultaneously and usually in quantities well below 0.5 ppm. Only in the case of DON have natural incidences of human foodstuffs contamination been occasionally encountered at levels well above 1 ppm (Pohland & Wood, 1987).

As noted earlier, soybean SDS can devastate tens of thousands of acres and cause million dollar losses. The causal fungus, *F. solani*, form A, has also been shown to produce a potent trichothecene mycotoxin, T-2 toxin, in culture. Although no reports have been published of T-2 toxin occurring in the beans of SDS-affected soybean plants, translocation of trichothecene mycotoxins from the roots to the shoots has been reported in at least one other plant species (Brosten & Simmonds, 1989). T-2 toxin has been rarely observed to contaminate foods although a mass poisoning incident did occur in the Oreburg district of the USSR in the 1930's, when it and related toxins caused approximately 30,000 human deaths from contaminated grain (Seagraves, 1981). T-2 toxin is better known to cause considerable contamination of animal feeds and farm animal toxicoses.

4. *Ergot toxins*. Two types of historical, fatal mass poisonings associated with mycotoxins are ergotism and ATA (discussed in previous section). Ergotism has occurred irregularly and reached epidemic proportions in the Middle Ages. It was characterized by a sensation of cold hands and feet, followed by an intense burning sensation, and eventually led to the extremities becoming gangrenous and necrotic. The notable outbreak of ergotism in humans occurred in Pont St. Esprit, France, in 1951, where considerable controversy still exists as to whether this local epidemic, traced to a certain batch of commercial flour, was due to ergot or mercury contamination or both (Wilson & Hayes, 1973).

Claviceps purpurea, the fungus responsible for causing the ergot disease of cereals and grasses, more often attacks rye than wheat. This fungus forms a large dark purple mass, containing an alkaloid ergotoxin, which has a

profound pharmacological effect on the human and animal body (Kent-Jones, 1986). Although human ergotism has a "long and cruel history," it has been of much less consequence in this century with changes in diet from rye to wheat and with improvements in grain quality. During the normal cleaning and milling process for grains, most of the ergot sclerotia are removed, leaving very small amounts of the alkaloids in flour (Pohland & Wood, 1987). In addition, the six naturally occurring, pharmacologically active alkaloids of wheat and rye ergots are relatively unstable: 59–100% destruction occurred in baking whole wheat bread, 50–85% in baking rye bread and 24–74% in preparing triticale pancakes (Scott & Lawrence, 1982).

Nevertheless, the ergot fungus is common enough to warrant study into its further reduction in grains and grasses. Various strategies have been advocated for ergot control. These include the use of resistant cultivars, cultural practices, and fungicides. Considered separately, none of these has clear potential of becoming fully effective; all aspects of control of this complex disease require attention in current research (Shaw, 1986).

Seed treatments with fungicides can reduce ergot infection of cereal crops. Seed treatment formulations of triadimenol and bitertanol mixed, respectively, with fuberidazole produced significant ergot reduction, compared to controls. The fungicides were applied to the surfaces of ergot sclerotia at the manufacturer's recommended rates for seed treatment, and percent germination data were collected following a winter period of seed burial in field soil. Further examination of the fungicide-treated sclerotia which did germinate revealed that production of fruiting bodies (ascocarps) was reduced in quantity and delayed in stage of development (Shaw, 1986).

B. Plant Defense Chemicals

Just as animals are able to defend themselves against predators, plants are naturally resistant to most surrounding pathogens. Many plants, upon contact with a pathogenic or non-pathogenic fungus, form antifungal compounds called phytoalexins (Dekker, 1986). For example, when *Botrytis cinerea* attacks a plant, the fungus secretes two types of compounds: pectin-degrading enzymes which are responsible for the structural degradation of the middle lamella and cell walls, and polysaccharides, which elicit the formation of phytoalexins (Kamoen, 1984). (The term "phytoalexin" was derived from the Greek to mean "warding-off agents in plants.") Phytoalexins inhibit growth or cause premature death of fungi and are toxic to many other biological species (Smith, 1982). *Botrytis* infections are often controlled with fungicides such as benomyl and iprodione, thus reducing hazards from phytoalexin production.

Although phytoalexins have potential for controlling insects and nematodes in addition to fungi, they may be toxic to higher animals and humans. It has been suggested that insects and diseases be warded off by selecting resistant crop varieties on the basis of their ability to accumulate toxic chemicals when stressed, but it must be realized that excessive induction of phytoalexins in a plant may cause phytotoxicity and other undesirable side-effects (Smith, 1982: Dekker, 1986). This has been a concern with white potato varieties genetically resistant to fungal diseases such as late blight. These varieties accumulate high levels of glycoalkaloids and terpenes because of stress or fungal infection (Wood, 1976; Kuc, 1977). Glycoalkaloids from potato cause lethal and teratogenic effects in chick embryos.

Several furanoterpenoid toxins have been isolated from fungal infected or blemished sweet potatoes. The most common of these plant defense chemicals (phytoalexins) is ipomeamarone (Catalano et al., 1977) which can occur at concentrations as high as 10,000 ppm in severely blemished and diseased sweet potatoes. This toxin has been shown to cause liver necrosis in mice and other animals (Wilson & Hayes, 1973). The common fungal pathogen, *Ceratocystis fimbriata* has been shown to markedly increase ipomeamarone levels in sweet potato tissue. This pathogen as well as *Rhizopus* and other fungi affecting sweet potato are controlled by the fungicides dicloran and sodium orthophenylphenate.

Moldy sweet potato toxicosis, characterized by severe pulmonary edema is caused by feeding cattle fungal infected sweet potatoes. The pulmonary toxins are not mycotoxins, but are formed when certain furanoterpenoid phytoalexins, produced as a result of fungal infection or other stress, are degraded by fungal pathogens. The 4 main lung-edemagenic furanoterpenoids are 4-ipomeanol, 1-ipomeanol, 1,4-ipomeadiol and ipomeanine. The presence of these toxins makes the consumption of fungal diseased sweet potatoes potentially dangerous to both human and animal health (Marasas et al., 1984).

Some phytoalexins (glyceollin, pisatin, ipomeamarone) have been shown to lyse (or disintegrate) red blood cells, as well as damage kidneys and livers in laboratory animals. Xanthotoxin occurs in diseased celery tissues and gives rise to blistering cutaneous disorders in humans when applied to skin in the presence of sunlight. This has been hazardous to fieldworkers harvesting celery and those handling celery in supermarkets. Coumestrol occurs in several legumes and possesses estrogenic activity in mouse uterine bioassays and may lead to infertility or other reproductive problems in sheep grazing on alfalfa or certain clovers.

A terpenoid phytoalexin called gossypol and its derivatives are the major terpenoids formed in the stem stele of *Verticillium dahliae*-infected cotton (Mace et al., 1985). The resulting cottonseed oil and meal containing gossypol and its derivatives are toxic to monogastric animals, including humans. Ruminants are not adversely affected (Smith, 1982). Gossypol is being tested as a male contraceptive in China (Arena & Drew, 1986).

These few examples have illustrated the potential hazards that may arise from natural defense chemicals when fungi attack crop plants.

IV. SUMMARY

Fungicides are critically important to farmers for protecting their crops from devastating fungal diseases. Less apparent to the public is the protection fungicides provide against toxin-producing fungi and fungal elicited toxic plant defense chemicals. These natural toxins can be a more serious health threat than the fungicide residues left on the produce. Therefore, responsible regulation must balance the risks of fungicide use against the risk of increased levels of fungal toxins and plant defense chemicals that will occur in foods if fungicides are not used.

CHAPTER 3

BEHAVIOR OF FUNGICIDE RESIDUES IN THE ENVIRONMENT

I. INTRODUCTION

Agricultural chemical use (fertilizers and pesticides) naturally results in soil and water contamination. When farmers apply pesticides, they expect them to affect pests or pathogens so that crop losses are minimal. However, it is inevitable that a certain portion of a pesticide application will miss not only the target pest or pathogen but also the plant. These so called non-target residues may end up on the ground, volatilize into the air, or drift to some other site. Pesticides are also applied directly to the soil in some cases to control insects, weeds, and pathogens. Since some of these chemicals can persist for extended periods of time, the possibility of their movement from soil into water systems and from both soil and water into organisms living in water and soil becomes a concern (Menzer & Nelson, 1986). Although most natural organic matter decomposes rapidly to carbon dioxide and water under the conditions favorable for biodegradation, some types can persist for extended periods of time when unfavorable conditions prevail. While the degradation rate of many synthetic organic pesticides is similar to that of natural materials, pesticide residues can be more persistent; some molecules or their metabolites may persist even under the most favorable conditions for biological attack.

Biodegradability must be defined in terms of the environment to which a pesticide residue is subjected (Sisler, 1982). The ultimate problem of pesticide residue persistence in the environment is whether the continued use of pesticides will eventually lead to long-term environmental contamination in amounts that may directly or indirectly endanger animals, plants or humans (Edwards, 1973). This chapter discusses fungicidal behavior in the environment, including environmental dissipation processes, rates and products of degradation from registered uses of fungicides.

Terminal sinks for most pesticide residues are water and soil. Three quarters of the earth's surface is covered by water, and the remainder that is not covered by structures, asphalt or concrete is covered by soil. Although water and soil are usually considered to be separate ecological systems, it is important to realize that suspended soil particles in water represent an interface between the two systems and serve as a mechanism for contamination of one by the other. The interface between soil and water is an intimate one; virtually all water systems contain suspended soil particles, and virtually all soil contains at least a small amount of water (Menzer & Nelson, 1986). Fungicide residues are seldom found in random environmental sampling of the air, water and biota. Generally, these chemicals are not very persistent because of their physical and chemical characteristics. Half-lives are usually short, but this can vary substantially depending on a number of factors including local environmental conditions. Further, the amounts of fungicides used are much less than insecticides and herbicides. Finally, because of their generally low non-target toxicity, fungicides have not been as actively sought in environmental monitoring programs as some other pesticides. Therefore, the ultimate fates of many fungicides have not been fully determined nor has the chronic environmental toxicity been evaluated.

The fate and distribution of chemicals in the environment are determined by several variables that can interact in numerous ways. The field of "chemodynamics" includes the study of a substance with respect to water solubility, soil absorption, vaporization, partitioning, bioaccumulation and degradation (Menzer & Nelson, 1986). Basic to chemodynamics are the following questions (Haque & Freed, 1974):

1) What are the properties of the compounds under consideration?
2) In what manner do the properties of the compound and of the environment determine the fate and behavior of the chemical?
3) To what extent does this determine the amount of the chemical to which humans and organisms are exposed?

In order to answer the question of what happens to a chemical when it is introduced into the environment, we must have an understanding of the nature of the environment itself and its fundamental phases: air (atmosphere), water (hydrosphere), land (lithosphere), and biota (biosphere) (Haque & Freed, 1974).

II. ATMOSPHERE

Residue concentrations in the atmosphere vary considerably among sampling stations within the same geographical region. Atmospheric pesticide concentration is a function of location of the pesticide application, wind direction, and atmospheric transport time.

Volatilization is a major pathway by which pesticides reach the atmosphere and move from treated plants, soil and water to other ecosystems. The amount and rate at which pesticide residues volatilize from leaves, soil or water depends on the chemical's vapor pressure, environmental conditions (especially temperature), plant surface structure, soil type and soil management practices. Not unexpectedly, pesticides volatilize more rapidly if they are applied to the soil surface rather then incorporated into soil (Pimintel & Levitan, 1986). In general, organic fungicides have low volatility and so it is unlikely that fungicide residues will be detected in the atmosphere except immediately after spray application.

Whenever an agricultural pesticide is sprayed on a field, there is initial migration of some of the active ingredient away from the target area. This takes the form of droplet drift at the actual time of spraying. Following the application, and extending over the next few hours, more of the pesticide may be carried off downwind if the active ingredient has sufficient volatility. Droplet drift is primarily dependent on the mechanical properties controlling dissemination and size spectrum of particles during application while vapor drift depends on the pesticide vapor pressure and the surface temperature of the target area (Maybank et al., 1978).

Dust particles in air can also absorb pesticides on their surfaces and be carried for considerable distances. Persistent pesticides can also be vaporized into the air from soil and water without evaporation of water.

Monitoring surveys of air in farming communities have indicated that pesticides used in these areas are present at low levels. Captan was one of six pesticides monitored in the air of three California communities. The captan residues shown in Table 3.1 are consistent with patterns of captan use in the vicinity of the communities studied (Seiber, 1987).

TABLE 3.1

SUMMARY OF CAPTAN AIR CONCENTRATIONS AT THREE CALIFORNIA SITES

Concentrations in ng/m³

Site	Maximum	Second Highest	Average All Positive Samples	No. Positive/ Total
Shafter	N.D.	N.D.	N.D.	0/11
McFarland	144	15.1	8.8	5/9
Pond	6.9	N.D.	6.9	1/12

* *Detection limit = 6.0 ng/m³*

Fungicides exhibit no unusual behavior in the atmosphere relative to other pesticide classes. Because fungicides, for the most part, are non-volatile, are neither acutely toxic to man and animals, nor phytotoxic, they have not been the subject of many atmospheric fate studies.

III. HYDROSPHERE

Although a number of insecticides and herbicides are commonly detected in the aquatic environment, fungicide residues are rarely found. Frank & Logan (1988) tested for residues of pesticides and industrial chemicals at the mouths of the Grand, Sangeen and Thames rivers in Ontario, Canada and found no evidence of fungicide residues, even though thousands of kilograms of captafol, captan and metiram are used for agricultural production annually in these river basins. One reason, perhaps, is that captan, captafol and metiram are degraded very quickly in water. Wolfe et al. (1976) reported that captan undergoes degradation in water with a maximum hydrolysis half-life of half a day. The products of the reaction were identified as sulfur, chloride ion and 4-cyclohexene-1, 2-carboximide. Once again, it should be pointed out that fungicides as a group are of little interest from the standpoint of water contamination because of their generally low toxicities to fish and other wildlife.

IV. LITHOSPHERE

Few organic fungicides are highly stable under a variety of conditions. Only hexachlorobenzene, which was formerly used for seed treatment, appears to rival the more stable chlorinated hydrocarbon insecticides in persistence. Half lives of several fungicides in non-sterile soil are given in Table 3.2. (The term "half-life" is used with some reservation; unlike the half-lives of radioisotopes that are constant and easily measured, the half-lives of pesticide residues in soil, water, plants, etc., are highly

dependent on rate of application and upon local conditions. Thus, there is no single, easily calculated value for the rate of pesticide residue degradation.) The important soil fungicide PCNB is quite stable and may persist in soil for several years (Sisler, 1982) (but is not in bioavailable form). The persistence of most other fungicide residues is considerably less. Benomyl and thiophanate-methyl may persist for 6 months to 2 years, depending on soil type, and thiram may persist for several months (Edwards, 1973). Benomyl is easily hydrolyzed in soil to carbendazim, a fungicide itself, whose residues may remain from less than three months to more than two years (Li & Nelson, 1985).

TABLE 3.2

STABILITY OF VARIOUS FUNGICIDES IN NONSTERILE SOIL

Fungicide	*Half-life (days)*	*Comments*
anilazine	2.5	application rate of 100 ppm in dry soil of pH 6.2
	0.5	application rate of 100 ppm in moist soil of pH 6.4
benomyl	90–365	based on total benzimidazole residues following application of 2.3–5.6 kg/ha
	90–180	metabolite MBC in vegetated soils
	180–365	MBC in bare soils (benomyl itself degrades rapidly)
captan	3–4	application rate of 100 ppm; initial soil pH of 6.4
	>65	application rate of 1000 ppm; initial soil pH of 5.7
	>50	application rate of 100 ppm in dry soil pH2 of 6.2
	3.5	application rate of 100 ppm in moist soil of pH 6.4
chloroneb	30–90	application rate of 2.25 kg/ha
chlorothalonil	>90	in moist soils; shorter half-life in dry soils
dichlone	>50	application rate of 100 ppm in dry soil of pH 6.2
	1	application rate of 100 ppm in moist soil of pH 6.4
fentin acetate	140	based on $^{14}CO_2$ released from 5–10 ppm aromatic labeled fungicide
iprodione	5–90	90% degradation in 5 days in extensively pretreated soils but 90 days in untreated soils
maneb	28–56	based on field samples
PCNB	117–1059	based on field samples
	>21	flooded (anaerobic soil)
thiram	>40	not detectable after 40 days at application rates of 250 ppm; more persistent at higher concentrations
triadimefon	15	in dry soil of pH 7.4
vinclozolin	75	soil pH of 5.7
	30–35	soil pH of 6.5

Sources: Burchfield (1959), Patil et al. (1988), Sassaman et al. (1986), Sisler (1982), and Walker (1987a,b).

The ultimate fate of many fungicides has not been fully determined. Environmental factors can have a marked effect on their biodegradation. Compounds which degrade readily in soils under favorable conditions for microbiological activity may persist for very long times in unfavorable environments. For instance, captan residues may remain in soil from one day to several months depending on soil type, temperature or moisture content (Buyanovsky et al., 1988). Moreover, interaction of a fungicide or its breakdown products with other substances, under certain conditions, can lead to the formation of hazardous or otherwise undesirable products (Sisler, 1982) as well as innocuous products.

The ethylenebisdithiocarbamate (EBDC) fungicides (maneb, mancozeb, nabam, zineb, etc.) provide a good example of this phenomenon. Oxidative reactions result in the formation of several degradation products from the EBDCs. Among these are ethylenethiourea (ETU) and ethylenebisisothiocyanate sulfide (EBIS). Studies have indicated that ETU is a goitrogen and a potential tumorigen and teratogen (Marshall, 1978) but it is not stable in soil (Kaars-Sijpesteijn & Vonk, 1970; Hylin, 1973).

Fungicide residues may influence the degradation rates of other pesticides as well. For instance, the presence of fungicide residues in soil can increase the half-life of the insecticide carbofuran by 1.2 to 3 times compared to carbofuran in isolation (Pussemeir, 1988). Fungicide residues have also been shown to increase the persistence of the insecticide parathion (Ferris & Lichenstein, 1980) but decrease the persistence of the fungicide captafol (Koeppe & Lichtenstein, 1982).

The recent development and widespread use of triazole fungicides has raised concern about their fate in the environment and the effects of these residues on mycorrhizal fungi associated with subsequent crops. Although not usually applied to soil, residues of these fungicides may reach the soil during foliar spraying, rain washing of the foliage and leaf fall. Patil et al. (1988) investigated the effects of chemical structure and physical properties on the rates of degradation of a series of ring-substituted 1-benzyltriazoles and compared these rates with those of triadimenol and PP450 (a fluorophenyl triazole derivative). For different ring substitutions, it was found that half-lives varied from 18 to 390 days. Furthermore, the observed stability of triadimenol and PP450 in soil agreed with previous results showing that these triazole compounds may be very persistent. Residues of triadimenol can control fungi the year following initial application and this prolonged selection pressure may result in the development of resistance in fungi to the fungicide.

The manner in which a fungicide is applied can also determine its persistence in soils. Griffith & Matthews (1969) reported that when captan and thiram were applied and well distributed in soil they had extremely low persistence, both having a half-life of between 1 and 2 days. By contrast, when glass beads were coated with these fungicides (to simulate their use as seed protectants) and subsequently mixed with soil, the persistence was much longer, with little change in the original concentration even after 21 days. This persistence could be explained by the relatively high concentration on the glass bead surface which could inhibit detoxifying organisms. Another possibility is that the surface area of fungicide exposed to detoxification was greatly reduced when present on the glass beads. These results help to explain the effectiveness of these fungicides as seed protectants despite their low persistence when mixed with soil.

Microbial degradation may be the single most important factor in preventing the buildup of pesticide residues, including residues of fungicides in soils, that otherwise could cause potential environmental problems. However, certain pesticide residues may be degraded so rapidly by soil microorganisms that their effectiveness is greatly reduced or even eliminated (Reed et al., 1987). For example, experiments with the dicarboximide fungicides iprodione and vinclozolin have shown that the rates of degradation were more rapid in soils previously treated with a particular fungicide than in untreated soils. The half-lives for the first and second applications of iprodione to soil were 23 and 5 days respectively (Walker et al., 1986). In another study of 33 soils from fields used for commercial agriculture, Walker (1987a) revealed that the time for 90% degradation of iprodione varied from less than 5 days in soils with extensive previous use of the fungicide to over 90 days in two previously untreated soils. This phenomenon is known as "enhanced" or "accelerated" microbial degradation. It is the result of the well known microbiological effect termed "selective enrichment" whereby the soil microfloral population is altered by the availability of a "new" nutrient, in this case the fungicide iprodione.

V. *MOVEMENT TO GROUNDWATER*

The movement of pesticide residues through a soil profile, termed "leaching", is one of the major characteristics of pesticide residue behavior in soil, and is controlled by factors such as soil type, absorptive capacity, moisture and percolation velocity. Leaching can take place in three directions: downward, due to gravity; upward, due to mass movement of water influenced by surface evaporation; and laterally, due

to discontinuities in the soil profile and other specialized factors. Upward movement may concentrate a residue at the soil surface, thus effectively removing it from the root zone (Haque & Freed, 1974). Water solubility of pesticide residues is another factor influencing their leachability, (Nicholls, 1988).

Rhodes & Long (1974) conducted greenhouse studies to determine the leaching and run-off characteristics of benomyl and its two soil metabolites, methyl 2-benzimidazole-carbamate (carbendazim) and 2-aminobenzimidazole, under rigorously controlled conditions (with simulated rain). Residues of benomyl and its metabolites were determined to be firmly bound to soil and did not leach or significantly move from the site of application.

Direct soil application and/or soil incorporation of pesticides are important factors contributing to groundwater contamination. By contrast, fungicides applied to foliage probably do not significantly contribute to soil and groundwater contamination. This is because oxidation and photochemical degradation on the leaf surface dominate the dissipation processes and residues that eventually reach the soil are low enough to allow for rapid degradation before leaching occurs.

In 1988, Oregon State University surveyed state agencies responsible for groundwater protection in the 50 states to determine the extent of groundwater contamination by pesticide residues used in agriculture. (No data from companies or the open literature were included.) The respondents categorized the results of residues found in groundwater over a range of values which could be used to evaluate the relative hazards of the findings. The resulting report cites 67 pesticide residues identified in 33 states (not all pesticide residues were found in every state).

Table 3.3 summarizes the results, including the number of states performing tests for a specific residue, the number of positive determinations, the number of wells tested, the number of negative findings, and the relative amounts found in the positive samples (Parsons & Witt, 1988). Of the 67 pesticide residues identified in 6032 positive samples out of 122,881 wells tested, only two were fungicides (chlorothalonil and PCNB).

TABLE 3.3

PESTICIDES DETECTED IN GROUNDWATER IN THE U.S.A.

Chemical	*St. test.*	*St. det.*	*No. of wells*	*No of wells found at* ND	0-1ppb	<HA	>HA
1, 2-Dicbloropropane	7	4	7035	6583		247	205
1, 3-Dichloropropene	5	4	5517	5510		2	5
2, 4-D	24	11	3758	3722	21	15	
2, 4, 5-T	9	3	842	836	4	2	
2, 4, 5-TP	13	2	2036	2020	16		
Aachlor	23	16	5016	4874	25	116	1
Aldicarb	21	11	4004	3418	5	407	175
Aldrin	12	3	1820	1815	1	4	
Atrazine	28	17	5569	4798	17	743	11
BHC	7	1	1320	1309		11	
Bromacil	4	3	726	720		6	
Carbaryl	10	1	1502	1497		5	
Carbofuran	18	7	1855	1769	7	76	3
Chloramben	5	3	400	392		8	
Chlordane	17	4	2046	2032	8	6	
Chlordecone	2	1	6	5	1		
Chlorothalonil	6	3	715	711	2	2	
Chlorpyrifos	11	2	981	978	3		
Cyanazine	19	10	3942	3875	3	62	2
DBCP	4	3	7040	4579	2	2335	124
DCPA	8	4	709	632	2	75	
DDD	5	1	1033	1031	2		
DDT	13	1	2071	2064	2	4	1
DEF	2	1	266	265		1	
Diazinon	14	2	1481	1473		8	
Dicamba	14	10	1239	1196	5	38	
Dicofol	4	1	792	791		1	
Dieldrin	13	3	1946	1938	7	1	
Dimethoate	7	2	916	914		2	
Dinoseb	10	4	1347	1308	1	30	8
Disulfoton	4	1	660	659		1	
Diuron	5	1	998	976		22	
EDB	12	9	5133	4534		79	520
Endosulfan	9	2	2839	2836	1	2	
Endrin	18	2	4305	4301		1	3
EPTC	6	2	1069	1063		6	
Ethyl Parathion	14	1	1106	1104	2		
Fonofos	8	1	2276	2275		1	
Heptachlor	13	1	2852	2850	2		
Hexachlorobenzene	5	1	1126	1122		4	

TABLE 3.3
continued

PESTICIDES DETECTED IN GROUNDWATER IN THE U.S.A.

Chemical	*St. test.*	*St. det.*	*No. of wells*	*No of wells found at ND*	*0-1ppb*	*<HA*	*>HA*
Hexazinone	6	1	198	197		1	
Lindane	15	5	3366	3350	6	6	4
Linuron	6	1	337	335		2	
Malathion	14	1	1347	1345		2	
MCPA	4	2	626	621		5	
Methamidophos	3	1	536	522		14	
Methomyl	9	2	1155	1152	2		1
Metboxychlor	19	3	2827	2822	3	2	
Methyl Parathion	11	1	1275	1269		6	
Metolachlor	19	11	2628	2540	16	71	1
Metribuzin	13	7	1900	1840	7	53	
Mirex	4	1	271	269	2		
Molinate	2	1	538	534		4	
Oxamyl	8	2	852	849		3	
p-Dichlorobenzene	1	1	1	0		1	
PCNB	4	1	304	303	1		
PCP	7	4	1518	1412	2	104	
Pendimenthalin	5	1	330	328	2		
Picloram	10	6	1028	990	10	28	
Prometon	4	3	418	406	2	10	
Prometryn	3	1	552	551	1		
Propachlor	5	2	702	699	1	2	
Schradan	5	1	103	93		10	
Simazine	17	10	2922	2819	3	99	1
Terbufos	7	2	794	792		2	
Toxaphene	11	3	3405	3396	6	2	1
Trifluralin	14	6	2636	2623	5	8	

ND = Not detected
HA = "Health Advisory," calculated from the fungicides ADI, based on 2 liters of water per day

This low incidence of fungicide residues is further described in Table 3.4. Residues of 14 fungicides were sought in the test samples but only two were detected — chlorothalonil and PCNB.

TABLE 3.4

LEVELS OF FUNGICIDES FOUND IN GROUNDWATER

Fungicide	*State*	*# Wells*	*ND*	*0-1 ppb*	*<HA*	*>HA*
benomyl	AR	20	20			
	CA	495	495			
captafol	TX	75	75			
captan	CA	712	712			
	TX	75	75			
carbendazim	CA	212	212			
chloropicrin	CA	795	795			
chlorothalonil	CA	490	489		1	
	MA	20	18	2		
	ME	88	87		1	
	OR	36	36			
	TX	75	75			
	WI	6	6			
dithiocarbamates	NH	15	15			
maneb	CA	268	268			
	CT	31	31			
metam-sodium	WI	23	23			
methyl bromide	CA	2874	2874			
	NJ	52	52			
PCNB	CA	165	165			
	MO	59	58	1		
	TX	75	75			
	WI	5	5			
triadimefon	CA	9	9			
zineb	CA	10	10			
ziram	CA	236	236			

ND = *Not detected.*
HA = *"Health Advisory," calculated from the fungicide's ADI, based on 2 liters of water per day; for chlorothalonil it is 105 ppb.*

Source: Parsons & Witt (1988).

Care must be used in interpreting the results presented in this report as representative of groundwater contamination nationwide since some states such as California have extensive monitoring programs, whereas other programs are small or non-existent. Furthermore, monitoring of groundwater for contamination by pesticide residues should be accompanied by core sampling and analyses. The absence of a pesticide residue in groundwater for several years after pesticide application does not necessarily mean the pesticide has degraded in the soil. It could mean that the residues are stable in soil and are leaching slowly but have not had time to reach groundwater. Therefore, carefully conducted soil core analyses are necessary to determine the potential for groundwater contamination from such residues (Cohen et al., 1984).

VI. BIOSPHERE

Our environment is a network of ecosystems involving more than 200,000 species in the U.S. alone. These biota perform many essential functions affecting agriculture, forestry and other aspects of human welfare. The application of pesticides can affect these natural ecosystems through non-target effects which may change the patterns of energy flow, nutrient cycling and reduced soil, air and water quality (Pimintel & Edwards, 1982). However the effect that the application of any pesticide has on the biosphere is primarily influenced by two independent factors: toxicity and persistence.

Modern fungicides and their residues are low in acute mammalian toxicity (Appendix B). For instance, benomyl is not very toxic to many forms of life (acute oral rat LD50 is greater than 10,000 mg/kg), but residues can persist for extended periods of time in an ecosystem. Furthermore, benomyl is toxic to fungi (after all, it is a fungicide!) and to earthworms, etc. Thus, while used for the control of pathogenic fungi, these compounds may be toxic to other microorganisms (Rajagopal et al., 1984) including beneficial and benign fungi. For instance, mycorrhizal fungi are thought to be beneficial components of many plant systems and fungicides, and their residues, that affect this association may adversely affect a plant's productivity (Trappe et al., 1984). Fungicides such as elemental sulfur, dinocap and benomyl may have deleterious effects on predacious mites and beneficial insects and thus, may interfere with the biological control of insect pests (Sisler, 1982). Frequent applications, over a period of time, of inorganic fungicides of relatively low toxicity, can result in soil accumulations which affect soil biota. In a survey of orchards in southeast England, those with a long history of heavy application of copper fungicides had very few earthworms and very poor soil structure (Edwards, 1973).

On the other hand, there may be beneficial non-target effects of fungicides. As one example, the benzimidazole fungicides (benomyl, carbendazim, thiabendazole and thiophanate-methyl) have inhibitory effects on parasitic mites (Upham & Delp, 1973) and nematodes (Miller, 1969).

VII. SUMMARY

Due to physical and chemical characteristics, fungicide residues, as a general rule, are not very persistent and are seldom found in random environmental sampling of the air, water and biota. They have not been as actively sought in environmental monitoring programs as other classes of pesticide residues because of the relatively small quantities of fungicides used and their generally low non-target toxicity. Ultimate fates in the soil and potential chronic environmental toxicity of many fungicides have not been fully determined. Their degradation is highly dependent on rate and type of application in addition to local environmental factors.

CHAPTER 4

FUNGICIDE RESIDUES IN FOOD

I. INTRODUCTION

In the United States the amounts of synthetic organic fungicides used in crop protection to control plant diseases are less than the quantities of insecticides and herbicides. The U.S. production of synthetic organic fungicides was 170 million pounds in 1960 and 109 million pounds in 1985, a decrease of 39% in 25 years. The comparable figure for insecticides was 366 and 370 million pounds (with a peak of 617 million pounds in 1970) and for herbicides was 102 and 756 million pounds (with a peak of 839 million pounds in 1981) according to the U.S. Bureau of The Census (1987). The trend toward lower amounts of fungicides reflects the development of systemic compounds which act on specific biochemical sites in disease-causing fungi. This high specificity results in lower rates of application with increased effectiveness for disease control (Gagnon, 1984). For example, the newest classes of systemic fungicides, the acylalanines and sterol inhibitors, are used at rates of ounces per acre as compared to pounds per acre for earlier fungicides such as captan.

The presence of pesticide residues on foods is often reported in somewhat alarming language, such as "nearly one-third of the apple samples were found to contain residues of one or more pesticides," or "fifteen different pesticides were detected in grapefruit" (Mott & Snyder, 1987). There is usually a level of exposure to any chemical which does not cause injury; pointing with alarm to the presence of a chemical without reference to the level of exposure is entirely without merit and creates a perception that there is risk when, in fact, a risk analysis has not been presented. In considering the significance of fungicide (or other pesticide) residues in food, an understanding of the basic elements of risk assessment is essential. These are discussed in Appendix C.

II. *NATIONAL PERSPECTIVES*

The criticism is often made that the regulatory agencies do not analyze for all the pesticides — that they only analyze for 200 or 275 out of 400 or 600 possible active ingredients. It is hard to imagine a more wasteful procedure than analyzing every crop for every pesticide that exists. The chemists at FDA and the state agencies are well aware of this. They know which pesticides are registered on each crop, which pesticides are recommended in each area, which pesticides are purchased and used in various areas and are quick to respond to information regarding local changes in use patterns, particularly to unregistered uses. They know how and when the pesticides are used on a particular crop, which ones disappear rapidly, which ones persist, and which ones to look for. To direct limited resources toward routine analyses for pesticides which almost certainly are not present would be extremely unproductive.

A. *Food and Drug Administration (FDA)*

FDA has conducted a monitoring program of the nation's food supply for pesticide residues since the 1930's. Data compiled from these monitoring efforts have shown that the U.S. population's exposure to pesticide residues is far below established tolerance (the legal maximum level of the residue of a particular pesticide permitted to remain on the crop) levels. In 1987, 14,492 samples were analyzed by the FDA, more than half of which were imported foods (mostly from Mexico). The results of their residue findings were published (Brown et al., 1988). Overall, no violative residues were found in more than 95% of the samples, and in 57% no residues were found at all. The FDA analyzed for residues of 253 pesticides, but only 113 (45%) were found in the 1987 monitoring program.

In addition selective surveys are used to determine the occurrence of a particular pesticide or a group of chemically related pesticides in a number of different crops, or they may focus on sampling one crop for one or more different pesticides. These surveys are generally aimed at food/pesticide combinations not normally covered as part of ongoing monitoring. In one selective survey sixty-one samples, representing 10 different foods, were analyzed for EBDC residues. No residues were detected in 28 of the samples (46%); 30 samples (49%) contained residues that were within legal limits. Three spinach samples (5%), all from the same grower, contained violative EBDC residues. The grower was advised of FDA's findings and voluntarily destroyed 25 cases of harvested spinach in two fields (Brown et al., 1988).

Data from over 25 years of FDA monitoring have shown that above-tolerance residues are rarely found, indicating that pesticide chemicals are generally used according to label directions. Although violative residues can result from misuse, unusual weather conditions, or poor agricultural practices, the most common cause is use of a particular pesticide on a commodity for which no residue level has been established.

Another major approach to monitoring used by FDA is the Total Diet Study, also known as the Market Basket Survey (or Study). The principal objective of the Total Diet Study is to develop dietary intake information on pesticides and compare it with the Acceptable Daily Intake (ADI). Of the more than 200 chemicals (pesticides, industrial chemicals, heavy metals, radionuclides, and essential minerals) that can be determined by various analytical procedures, 64 different pesticides and industrial chemicals were found in each market basket of 234 foods between 1982 and 1984, and 53 pesticides in the 1987 market basket survey. Both times the most commonly found fungicide residue was that of dicloran: 108 findings out of 1,872 samples (6% occurrence) in 1982-84, and 41 findings out of 936 samples (4%) in 1987. The other most frequently occurring fungicide was PCNB (quintozene): 20 findings (1% occurrence) in the first study and 32 (3%) in the second (Brown et al., 1988; Gunderson, 1988). Table 4.1 lists the reported fungicide intakes for three of the eight U.S. population groups covered by the study and their corresponding Acceptable Daily Intakes (ADIs), in order of decreasing occurrence. The comparisons show that the dietary intakes of pesticide residues are consistently below established ADIs, in most cases by orders of 100 to 1000 fold. (As explained in Appendix C, the ADI generally provides a safety margin of about 100.)

TABLE 4.1

FUNGICIDE ADIs AND INTAKES FOUND IN TOTAL DIET ANALYSES FOR THREE AGE/SEX GROUPS

Fungicide	*ADI*	*Intake by Age / Sex Group* 6-11 mo.	14-16 yr. M	60-65 yr. F
captan (1982–84)	100	0.0361	0.0156	0.0425
captan (1987)	100	0.0194	0.0088	0.0244
chlorothalonil (1987)	3	<0.0001	<0.0001	0.0001
dicloran (1982–84)	30	0.2560	0.0515	0.1351
dicloran (1987)	30	0.2767	0.0682	0.1793
folpet (1987)	10	0.0078	0.0029	0.0096
iprodione (1987)	300	0.0064	0.0025	0.0038
PCNB (quintozene) (1982–84)	7	0.0023	0.0033	0.0017
PCNB (1987)	7	0.0011	0.0011	0.0005
vinclozolin (1982–84)	40	0.0078	0.0031	0.0094
vinclozolin (1987)	40	0.0121	0.0044	0.0145

ADI = Acceptable Daily Intake
ADIs and intakes are expressed as 10^{-6} g/kg body weight / day.
Sources: Brown et al. (1988) and Gunderson (1988).

FDA also compiles and summarizes data on foods analyzed by states for pesticides (and industrial chemicals). In this system, known as "FoodContam," results for about 15,000 samples were received in 1988 from five states: California, Florida, New York, Virginia, and Wisconsin. These data indicate that dietary intake is usually well below 1% of the ADI.

B. *California Department of Food and Agriculture (CDFA)*

Pesticide residue monitoring is also performed at the state level. At least 38 states have such programs although there is considerable variation in scope. The most extensive pesticide residue monitoring program in the U.S. exists in California, which is the country's most agriculturally productive state (agricultural production income exceeds that of the next leading state by 45%). State and county pesticide regulatory expenditures total more than $40 million annually, which is approximately the same annual budget as that of the EPA Office of Pesticide Programs (Ridley, 1988). CDFA routinely samples commodities offered for sale in the state from chain store distribution centers, wholesale markets, retail shelves, and points of origin (packing houses and farmers' markets). This monitoring program is larger than the one operated by the federal government. CDFA also analyzes commodities imported from foreign countries. Through the use of the

Multi-Residue Screen analytical methods, it is possible to analyze for more than 100 of the most frequently found pesticides (Stimmann, 1988).

The CDFA residue data are consistent with other data showing both infrequent appearance and low levels of fungicide residue. For the fungicide captan, the residues found in monitored commodities were generally well below the anticipated residue (in fact, usually below the levels of detectability), with an infrequently high value on a minority of samples (see Table 4.2). For cherries, monitoring resulted in finding that over 96% of the samples had less than one ten-thousandth of the tolerance level of captan.

TABLE 4.2

COMPARISONS BETWEEN CURRENT TOLERANCE, ANTICIPATED RESIDUE AND RESIDUE DATA FROM CALIFORNIA'S MONITORING PROGRAM FOR CAPTAN RESIDUES IN VARIOUS COMMODITIES, 1981-1984

Commodity	*LLD* [a]	*MFOL*	*(%)* [a]	*MOL* [a]	*AR* [a]	*CT* [a]
almonds	0.01	<0.01	(100%)	0.0	0.14	2.0
apricots	0.01	<0.01	(98%)	5.0	4.98	50.0
cherries	0.01	<0.01	(96%)	20.0	18.56	100.0
grapes	0.01	<0.01	(84%) b	50.0	4.49	50.0
nectarines	0.01	<0.01	(100%)	0.0	2.17	50.0
peaches	0.01	<0.01	(98%)	10.0	6.59	50.0
plums	0.01	<0.01	(100%)	0.0	1.8	50.0
strawberries	0.01	<0.01	(72%) [c]	20.0	5.39	25.0

N.B.: All residue values given in parts per million (ppm).

[a] *LLD = Limit of Detection (smallest amount of captan residue that can be accurately detected with current laboratory practices.)*

MFOL = Most Frequently Observed Level (the residue level most often observed in CDFA monitoring data during this time. The number in parentheses indicates the percent of samples at this level.)

MOL = Maximum Observed Level (the maximum residue observed in the monitoring data.)

AR = Anticipated Residue (the average residue in samples from controlled field trials where captan was applied at the maximum rate permitted and samples were collected the minimum number of days permitted between the last application and harvest.)

CT = Current Tolerance (maximum allowable residue established and published by EPA and used by FDA for enforcement.)

[b] *In this commodity 99% of samples contained <5.0 ppm.*

[c] *In this commodity 92% of samples contained <5.0 ppm.*

Source: TAS, 1987.

In 1987 the CDFA analyzed a total of 7,010 samples of raw agricultural commodities destined for the marketplace. No pesticide residues were detected on 79.8% of these samples. Residues within the legal tolerance limit were found on 18.7%. Thus, 98.5% of the samples were either without detected residues or were within tolerance level. The remaining samples with illegal residues accounted for only 1.5% of all samples analyzed: 1.2% of the samples had residues of pesticides for which no tolerance was established (i.e., for which any detectable residue was illegal), and the other 0.3% had residues exceeding tolerance levels. Appendix D lists the fungicides that were detected by the CDFA in their routine monitoring program. Though some do not, most detected residues fall within the established tolerance levels.

Since analysis of random commodity samples might omit some pesticides of particular concern, the CDFA sets priorities for a "focused" monitoring program by targeting those pesticides which are associated with known or suspected health concerns. In this focused monitoring program, pesticides whose use has been identified as a possible health concern are targeted for more specific monitoring by sampling commodities from fields known to have been treated with them, using the species specific residue test method. In this way, the presence of residues can be predicted and their likely levels calculated (Stimmann, 1988). When residues are found there is no question that the amounts are from a treated commodity and not from pesticide drift. Appendix E lists all pesticide residues detected in the focused monitoring program. (Additional information on CDFA monitoring may be found in Appendix F)

C. *Private Industry*

Government agencies are not the only groups testing for pesticide residues in food. Chemical companies also conduct their own research. In response to the EPA's special review of EBDC fungicides, Rohm and Haas has performed a number of market basket surveys to test for residues. Over 1,000 samples of fresh and processed fruits and vegetables were analyzed for residues of both EBDCs and ETU, a degradation product. The analytical methods measured all EBDCs simultaneously and additively. Results showed that 898 out of 1,011 samples (89%) contained no detectable residues of EBDC fungicides (limit 0.2 ppm). For ETU, 941 out of 974 samples (97%) contained no detectable residues (limit of at least 0.05 ppm). When residues were found for either two compounds, they were almost always at or slightly above the detection limit (Larkin, 1987).

D. *The Fallacy of Exaggerated Risk from Exposure to Residues*

There is a considerable difference between the amount of residue actually found in foods by federal and state regulatory agencies in their monitoring and surveillance programs and the amount permitted in the tolerance. Actual residues are generally much lower. The tolerance value is necessary for enforcement purposes but of little value in risk assessment (TAS, 1987). In actual practice the federal and state regulatory agencies report that fungicides are seldom found in foods and when found are usually far below the tolerance.

EPA asked the Board on Agriculture of the National Research Council (NRC) to study the EPA's methods for setting tolerances for pesticide residues in food. The National Academy of Sciences (NAS) published their report in which risk calculations were made based on the assumptions that (1) all residues were present at the published Code of Federal Regulations tolerance levels, (2) all (or nearly all) of the pesticides registered for use on a crop were used on that crop, and (3) 100% of the acreage of that crop was so treated (NAS 1987b). One could easily predict that such an extremely exaggerated residue level scenario would result in very high risk levels, and indeed this was the result. Unfortunately the press focused on the unrealistic risk projections.

The NAS report did not calculate the risk for all registered pesticides, but did include all pesticides that were considered possibly oncogenic for which cancer potency factors were available. The fungicides in this group were benomyl, captafol, captan, chlorothalonil, folpet, fosetyl-Al, mancozeb, maneb, metiram, o-phenylphenol, and zineb. The report presented conclusions showing rather high cancer risks from pesticides in foods, and in particular from fungicides. For example, the total cancer risk from pesticides in foods was presented as 5,800 per million; of that 3,500 per million was attributed to fungicides (or 60% of the risk), and for the single food, tomatoes, the risk presented was 875 per million for all pesticides and 823 per million for fungicides alone (NAS, 1987b). The high levels of risk resulting from calculations using exaggerated residue levels in conjunction with scientifically questionable carcinogenicity assessment methodology have created unnecessary alarm among many consumers.

The data for tomatoes were recalculated (Archibald & Winter, 1989) using actual residue and incidence data from the Los Angeles FDA laboratory and revealed that the cancer risk from pesticide residues on tomatoes was only 0.33 per million. For the total of all fungicides detected (captafol, captan, chlorothalonil, folpet and o-phenylphenol) the risk was 0.24 instead of the 334 per million that would be the estimate from the calculation procedures used by the NRC. The lower

risk levels are due to the facts that actual residues are less than the tolerance value, and every fungicide is not used on 100% of the tomato crop. For that matter, every fungicide is not used even on small segments of the tomato crop.

To place the risk values obtained by the NRC and Archibald and Winters in perspective, one should be aware that when a valid risk number is as high as 1 per 1,000 (1,000 per million) the risk is considered to be intolerable and immediate corrective action must take place. When the risk number is as low as 1 per million, the risk is considered to be so low as to be an improbable occurrence. The NRC risk values could best be described as the theoretical maximum risk, but because their exposure assumptions relating to frequency of use and level of residues are so deliberately exaggerated the results have no relation whatsoever to actual risks. The project officer for the NRC report has agreed that the risk value for pesticide residues on tomatoes is exaggerated and his informal estimate is that the actual value should be "1, or possibly 2, per million" (Wiles, 1989, pers. comm.). For fungicides on tomatoes the NRC grossly overestimated the risk. Similar overestimations were made for other crops and other pesticides.

III. EXAMPLES OUTSIDE THE U.S.

Between 1980 and 1985, 354 composite vegetable samples representing nine vegetable commodities (asparagus, beans, carrots, cauliflower, cucumbers, onions, potatoes, sweet corn, and tomatoes) were collected from farm deliveries to the market place in Ontario, Canada. All samples were analyzed for insecticides, 275 for fungicides and 135 for herbicides. In most samples, pesticide residues were below the detection limits (i.e., at levels of 0.005 to 0.1 parts per million) and most of the positive findings were a fraction (i.e., <1–20%) of the maximum residue limit (MRL) permitted for each commodity under the Canadian Food Drugs Act and Regulations (similar to the U.S. federal tolerance limits). Fourteen samples (4% of total) had residues exceeding the MRL; none were fungicides (Frank et al., 1987a). The fungicide residues were well within the margin of safety. Captan was identified on tomatoes at 0.6% of the 5 ppm tolerance; chlorothalonil was found in cauliflower, cucumbers and tomatoes at also a fraction of the respective MRLs (0.2–8.4% of tolerance). No acylalanine fungicides (such as metalaxyl) were detected above the 0.01 ppm limit. Dithiocarbamate fungicides (maneb, ziram, thiram, etc.) were identified in cauliflower, cucumbers and tomatoes, though at low residue levels (2.5–14% of tolerance). No other fungicides were detected (Frank et al., 1987).

In a description of Canada's Federal Interdepartmental Committee on Pesticides Check Sample Program, Conacher (1987) listed the average residue values of captan and iprodione in strawberries. In both cases they were well below the allowable tolerance level by an order of magnitude: captan residues averaged 2.5 ppm (25 ppm tolerance) and iprodione residues were 1.1 ppm (15 ppm tolerance).

Seed treatments with fungicides result in high residue levels associated with the treated seed; thus, they must not be consumed. However, fungicide levels reaching the soil or the new crop are quite small. For example, residues of thiophanate-methyl and maneb in wheat grain in Belgium were not detectable with an LLD of <0.03 and <0.1 ppm, respectively (Hormann, 1980).

The EBDCs are an important group of fungicides. Zineb and maneb (and propineb in Europe), for instance, are widely used in viticulture for downy mildew control (Casanova and Guichon, 1988), and maneb is used in hops to control *Peronospora* prophylactically (Nitz et al., 1984). Recent analyses (Casanova and Guichon, 1988) of 1987 and 1988 French wines (Bordelais, Savoy, Touraine, and Beaujolais) and of commercial beers (from Belgium, Denmark, France, Great Britain, Ireland, and West Germany) showed that none of the samples contained EBDC fungicide residues above the 0.15 ppm detection limit. Furthermore, 77.4% and 91.8% of the beer and wine samples respectively were under the limit of detection of ETU (0.01 ppm). In Germany, particularly, legislation (specification of maximum number of applications and establishment of a 28-day preharvest interval) in the early 1980's concerning hops spraying has evidenced a drastic reduction of ETU in beer so that now virtually all of that product is well below the FAO/WHO recommendation of 0.1 ppm (Nitz et al., 1984).

IV. POST-HARVEST FACTORS AFFECTING RESIDUE LEVELS

Most of the concern regarding pesticide residues is focused on raw agricultural commodities, particularly the many fruits and vegetables people purchase daily in grocery stores around the country. However, much of what is bought is already processed. Apples, for instance, appear in stores not only as fresh fruit, but also in canned, spiced, frozen, dehydrated, jellied or juiced products. Apples also appear in candies, breakfast cereals, and other food forms (TAS, 1987).

In most cases processing reduces pesticide residues; in others, however, conversion products may accumulate (as in the case of EBDCs being converted to ETU.) It is well documented (Newsome and Laver, 1973;

Phillips et al., 1977; Nitz et al., 1984; NAS, 1987b; and many others) that EDBCs can degrade to ETU (ethylenethiourea) during cooking. ETU formation is important to monitor because of its possible hazard to man. Due to the nature of ETU analysis, initial positive results by gas chromatography should be considered highly suspect (i.e., as a false positive) until confirmed by a second analytical method, preferably gas chromatography/mass spectrometry. Phillips et al., (1982) reported that only two of 21 initially positive ETU results were confirmed by repeat analyses.

Although many investigations have shown that significant accumulation of ETU does not occur on the surface of treated plants due to its rapid photooxidation to ethyleneurea (EU), residues of EBDCs can be converted into ETU either during industrial processing involving heat treatment or in other processing operations. In investigating the thermal conversion of mancozeb to ETU in the course of apple processing, Hajslova et al. (1986) found that ETU formation was reduced at lower pH values, as well as in the presence of an antioxidant (ascorbic acid [vitamin C] or cysteine). However, the antioxidant inhibited ETU's decomposition when it did appear.

Koivistoinen et al. (1965) studied the effects of various food processing methods on captan residues and determined that if the process included a heating phase, losses were usually over 90%. For instance, canning gooseberries reduced levels by 98%, and gooseberry jam had almost no detectable residues. Freezing string beans reduced levels by 86 to 90%, depending on storage time (<1–8 months). Canned plums, dried plums, and plum jam all had losses of 98% or more, as did pasteurized apple juice. Fresh juice had 88% loss of captan.

Fungicide residues are also affected when grapes are processed into wine. De Chaunac grapes treated with a single application of captan had residues of 3.2 ppm in the fruit. Eight days after this treatment the destemmed grapes had 2.2 ppm captan, and the stems 16 ppm; crushing the grapes reduced it to 1.9 ppm. Six days thereafter, the pressed, fermented juice (skins and seeds removed) had no detectable captan to a limit of 0.01 ppm, and no residues were found in the finished wine 244 days later (Frank et al., 1985).

Pesticide residues are also frequently dissipated or stripped from the edible product during routine agricultural and marketing procedures. For example, Cabras et al. (1988) reported that when chlozolinate, a new dicarboximide fungicide that is active against *Botrytis cinerea*, was applied to outdoor crisp head lettuce, residues in the internal, edible leaves were much lower than those in the wrapper (external) leaves,

which are routinely discarded at harvest for esthetic and commercial reasons. After treatment with the fungicide, external leaves had 6.78 ppm, whereas internal leaves had only 1.75 ppm. Seven days later, the external residue was 3.29 ppm, while internal leaf residues were 0.66 ppm. This same reduction of residue levels as a result of harvesting and handling occurs when celery is treated with chlorothalonil as shown in Table 4.4.

TABLE 4.4

CHLOROTHALONIL RESIDUES IN CELERY

Sampling Location	*Residues (ave.) ppm*	*% of Field ppm*	*% Residue Removed*	*% of Tol.* [a] *in Steps*
Field	2.3	100	0	15.3
Packing House	1.3	57	43	8.7
Grocery	0.5	22	62	3.3
Restaurant	0.1	4	80	0.7

[a] *Tolerance is 15 ppm*

Source: TAS. 1987

Reduction of residue levels is not limited to industrial processes and harvesting techniques. Most people wash fruits and vegetables before eating or cooking to remove ordinary dirt and dust. This practice can also reduce pesticide residues. The most commonly detected fungicide residues include captan, chlorothalonil, dicloran, diphenylamine, iprodione, thiabendazole, and vinclozolin, most of which can be reduced or eliminated by washing (Mott and Snyder, 1988). The amount by which washing and cooking reduce residues can be considerable. Studies show that washing tomatoes under running tap water reduced captan residues by 97.7–98.9%. Similar levels were obtained by cooking tomatoes for 15 minutes without washing. Also, washing and cooking treatments reduced folpet residues by 93.7– 97.5% and 95.0–98.1%, respectively (El-Zemaity, 1988).

Residues most easily removed by washing, particularly with only water, are called dislodgeable residues and are a result of recent pesticide applications using wettable powders or flowable formulations rather than an emulsifiable concentrate. When a pesticide residue equilibrates in the cuticular waxes or penetrates into the epidermal cells it will not be easily removed by simple rinsing.

Northover et al. (1986) reported that tumble washing for as little as 15 seconds removed captan residues on Bing sweet cherries by 70–74%, and

by 93–97% after two minutes. This means that in one trial, when initial residues were at 2.7 ppm (far below the allowable 100 ppm tolerance), 15 seconds of washing reduced captan levels to 0.8 ppm, and two minutes of washing to 0.2 ppm. In another trial, originally at 6.8 ppm., 15 seconds of washing reduced captan levels to 1.8 ppm, and two minutes' washing to 0.2 ppm. Koivistoinen et al. (1965) also reported captan losses (some of them substantial) on gooseberries, plums, tomatoes, apples, and string beans, as a result of washing under running tap water for 30–60 seconds. Washing also removed significant amounts of both EBDC and ETU residues on tomatoes and carrots, though on western spinach (which had excessive EBDC residues even before washing) residues still exceeded tolerance levels (Phillips et al., 1977).

V. *SUMMARY*

Fungicides applied in the production of food seldom result in detectable residues in food. When fungicide residues are found in food, they are usually orders of magnitude less than the allowable tolerances (levels considered safe). Processing and handling of commodities generally reduce or eliminate fungicide residues from the levels detected on field harvested samples, on which measurements are made to assure compliance with the tolerance or acceptable residue levels. Providing a safe food supply is not a static process and requires continuing review of the occurrence of pesticide residues, examination of new toxicological data, and the evaluation and use of new risk assessment methodology. These processes are constantly carried out by federal and state regulatory agencies, universities, private corporations and other groups.

CHAPTER 5

EXPOSURE OF AGRICULTURAL WORKERS TO FUNGICIDES

I. INTRODUCTION

The 1985 accident rate in farming (12.7 cases per 100 full-time workers) was second only to that in construction work (Widome et al., 1988). Farming is considered hazardous in other countries as well. Denis (1988), Cryer & Fleming (1987) and Jansson & Jacobson (1988), for example, describe farming hazards and injuries in Canada, New Zealand, and Sweden, respectively. The most common cause of injuries is from farm machinery. Farm workers also have the highest rates of all industry groups for skin diseases and poisoning. Chemical products used in farming were at one time assumed to affect only plant, insect and animal life. However, they have come increasingly under scrutiny because of the potential for harmful effects in humans (Cordes & Rea, 1988).

In analyzing surveys of occupational injuries, however, it is important to keep the various causes in perspective. A recent survey (Langworthy & Maligro, 1987) of such injuries on a large pineapple plantation in Hawaii during the harvest season showed that physical injuries occurred much more frequently than injuries caused by chemical exposure. Dermatitis, the only illness or injury thought caused by exposure to chemicals, accounted for only 3.3% of the cases reported.

II. *FARM-WORKER ILLNESSES REPORTED IN CALIFORNIA*

The state of California has the most diverse agricultural environment of any of the 50 states and, in a number of cases, grows the majority if not the total U.S. production of certain crops. This diversity, coupled with the acknowledged hazards of farming and very active farmer and farm-worker interest groups, has resulted in pressure on the state government to monitor accidents and illnesses occurring on the farm.

In compiling its statistics, the California Department of Food and Agriculture (CDFA) evaluates each reported pesticide-related illness based on information from investigative reports, physicians' reports, and toxicological and medical data. If sufficient information is available, the relationship is categorized according to the following scheme (Edminston & Richmond, 1988).

1) Definite: high degree of correlation between the pattern of exposure and the resulting symptomology. Medical tests and physical evidence have been collected and support the conclusion.
2) Probable: relatively high degree of correlation exists between pattern of exposure and illness experienced. Medical and/or physical evidence is absent.
3) Possible: some degree of correlation evident. Work history and/or application history ambiguous.
4) Unlikely: a correlation cannot be absolutely ruled out. Work history and/or application history minimal and ambiguous.
5) Unrelated: no correlation between the pattern and alleged exposure and the resulting illness.

In 1987 there were a total of 2,897 possible pesticide-related illnesses reported to CDFA. Of these, 1,754 (40%) were determined to be related to pesticide exposure: 1,507 occupationally related and 247 non-occupationally related. The remainder were determined to be unrelated to pesticide exposure. Table 5.1 lists which of the 1,507 reported, occupationally related pesticide illnesses were best linked to exposure to

fungicides. If the cases thought due to exposure to sulfur (which accounts for 44% of the cases) are subtracted, because sulfur is an acaricide and an insecticide in addition to having antifungal activities, 130 cases are left (8.6% of the occupationally related illnesses) as due to exposure to fungicides or fungicide residues.

TABLE 5.1

FUNGICIDES REPORTED AS CASUAL AGENTS IN OCCUPATIONAL ILLNESS/INJURY INCIDENTS IN CALIFORNIA, 1987 FROM 1,507 TOTAL REPORTS FOR ALL PESTICIDES

Fungicides	*Systemic*	*Eye*	*Skin*	*Eye/Skin*	*Total*
anilazine	0	0	1	0	1
benomyl	1	0	2	0	3
benomyl, captan, dienochlor, fenbutatin-oxide	0	0	3	0	3
benomyl, captan, formetanate hydrochloride	0	1	1	0	2
captan	1	1	3	1	6
captan, sulfur	0	0	5	0	5
carboxin	0	0	1	0	1
chloropicrin	1	3	0	0	4
chlorothalonil	0	1	4	1	6
copper	0	0	1	0	1
copper 8-quinolinolate	0	0	2	0	2
copper naphthenate	2	1	1	0	4
copper oxychloride sulfate	1	0	0	0	1
copper sulfate	1	3	1	1	6
dodemorph acetate	1	0	0	0	1
fenarimol	0	0	1	0	1
folpet	0	1	0	0	1
formaldehyde	0	1	0	0	1
imazalil	0	0	1	0	1
iprodione	1	0	1	0	2
lime-sulfur	2	0	0	0	2
mancozeb	1	0	0	0	1
maneb	0	0	4	0	4
maneb, metalaxyl methamidophos	3	0	0	0	3
maneb, sulfur	0	0	2	0	2
metalaxyl	0	0	1	0	1
metham-sodium	0	0	2	0	2
sodium arsenite	1	0	0	0	1
streptomycin	0	1	0	0	1
sulfur	12	14	75	3	104
sulfur, triadimefon	2	1	5	1	9
sulfur dioxide	1	1	1	0	3
triadimefon	9	3	1	0	13
triforine	1	0	0	0	1
ziram	1	0	7	15	23
misc. fungicides	1	8	3	0	12
TOTAL	43	40	129	22	234

** Includes those cases with an exposure / illness relationship of Definite, Probable, or Possible.*

Source: Edminston & Richmond, 1988.

III. MODES OF EXPOSURE

Direct exposure to formulated pesticides may occur whenever these chemicals are handled during (Coutts, 1980):

1) formulation at the production plant.
2) transport to distribution centers, the end user's storage facility and to the application site.
3) transfer from container to application equipment.
4) application of the pesticide to the treatment site.

Exposure to pesticide residues can occur during:

5) contact from drift of pesticides outside the intended area of application.
6) contact with treated plants during field work and at harvest.
7) post-harvest contact during packaging.

Contact can be dermal (to the hands or other parts of the body) or respiratory (through the breathing of vapors or airborne particles, which may be either pesticide residues or soil dust particles containing absorbed residues). Many studies show that the hands are the most exposed body part during mixing/loading operations and spraying. For example, in a study of U.K. workers spraying a cereal crop with the fungicide prochloraz, Bonsall (1985) found 99% of their exposure occurred during mixing and loading. Gloves received 97% of the total body surface contamination during both filling the tank and subsequent spraying. A working day of eight hours spent repeatedly filling a tank and then spraying the crop was calculated to provide a potential respiratory exposure of, at most, 0.5 to 1.4 mg of the pesticide active ingredient. Therefore, dermal exposure can be significant to those who work with pesticides in the field. Protective clothing provides the most important means for minimizing exposure to pesticides during mixing/loading, application, inspection of recently treated fields and other pesticide operations (Morsaki & Nielsen, 1985). Unfortunately, many workers resist wearing conventional protective garments because of the discomfort resulting from the garment's low moisture and air permeability. Common reasons given for not wearing protective clothing or equipment are: "It's too hot." "It's too uncomfortable." "It's not provided." "It slows me down." "I don't know how to use it." (Moses, 1988).

As a result of this problem, Norton et al (1988) investigated the exposure protection offered by an experimental Gore-Tex spray suit during orchard spraying, as compared to a commercially available suit. No measurable trace of dinocap or mancozeb was found on inside

patches in any suit, though deposition on outside patches was often considerable (as high as 20 micrograms/cm^2 on the chest and 32 micrograms/cm^2 on the shoulders). Because Gore-Tex outfits breath well, they make protective and comfortable spray suits. A less costly alternative to Gore-Tex is 100% cotton denim coveralls. Davies et al. (1982) studied their effectiveness on applicators and mixers of ethion in Florida citrus groves. Not only did the cotton coveralls provide excellent protection, but they were completely satisfactory to the workers, several of whom expressed appreciation of the coolness of the cotton fabric and attributed it to the fact that the 100% cotton cloth readily absorbed their perspiration and cooled them off. The same could not be said of respirators, which produced heat and discomfort due to sweating around the face mask, as well as a rash resulting from excessive sweat.

Investigations of short-term pesticide exposures have shown that used pesticide containers may be a source of problems. Disposal of these items when empty may be difficult, since often they are large, sturdy, nonrefundable, metal drums or attractive, plastic cans and bottles that can be improperly reused as storage barrels for water, trash, harvesting and transporting crops, and as storage barrels for water, trash, harvesting and transportating crops, and as children's toys (Moses, 1988). According to Moses' survey (1988), few field workers knew the names of the pesticides to which they had been exposed. For example, 75 workers out of 105 claimed they had been exposed, but only 21 could be specific and name the particular pesticide. Only one of 29 pesticides mentioned by workers could possibly be classed as a fungicide (sulfur).

IV. EXAMPLES OF EXPOSURE TO FUNGICIDES

Mines & Kearney (1982) surveyed farm workers in Tulare County, CA for symptoms the workers believed were caused by agricultural chemicals. As listed in Table 5.2 rashes and itches were the major symptoms (46%) followed by headaches (44%) and irritated eyes (27%).

TABLE 5.2

HEALTH PROBLEMS
THOUGHT TO BE CAUSED BY CHEMICAL EXPOSURE

Problem	*Frequency*	*Percent*
Rash or itch	194	45.5
Headache	189	44.4
Irritated eyes	113	26.5
Dizziness	104	24.4
Sweaty hands	78	18.3
Nausea	74	17.4
Muscle twitches	56	13.1
Fainting	35	8.2
Sore throat	11	2.6
Irritated lungs / cough	9	2.1
Irritated nostrils	5	1.2
Fatigue	4	0.9
Diarrhea	2	0.5
Loss of appetite	2	0.5
Swelling	2	0.5

N = 426. (Some individuals responded positively to more than one complaint.)

Source: Mines & Kearney (1982).

Fenske et al. (1987) concluded that dermal exposure to pesticides in greenhouses can probably be reduced substantially by (1) greater forearm protection, (2) the use of face shields during both mixing and application, and (3) thorough washing of clothing following each work period.

The role of the respiratory route as a source of pesticide exposure has been studied in the past by both direct and indirect methods but little has been done in comparing exposures from different activities. Respiratory uptake is a significant problem in the leaf cutting operation of grape cultivation, where the potential for sulfur inhalation is great (Mines & Kearney, 1982).

Oudbier et al., (1974) studied routine exposure operations on a farm in southwestern Michigan where farmers utilized air-blast speed sprayers drawn by tractors for pesticide application. Analysis of respirator filter pads worn by workers in the field indicated that in 8 out of 11 paired mixing and spraying operations, greater total amounts of detectable pesticides were found on pads used in the mixing activities regardless of the time involved. Thus, it was apparent that the period of pesticide

mixing and tank filling presented the greater potential hazard of respiratory exposure. Table 5.3 shows the amount of captan detected on respirator pads in the study. (Wettable powder formulations were apt to cloud in the operator's face when the bag was opened and dumped into another container for weighing or directly into the tank hatch opening.)

TABLE 5.3

RESPIRATOR PAD ANALYSIS
OF CAPTAN USED IN THE FIELD

Operations	*Quantity Found (ng)*	*Exposure Time (min)*	*Rate (ng/min)*
Mixing	97,150	5	19,430.0
Spraying	12,395	39	317.8
Mixing	4,620	6	770.0
Spraying	8,820	38	232.1
Mixing	16,800	8	2,100.0
Spraying	9,800	24	408.3
Mixing	4,788	3	1,596.0
Spraying	15,750	24	656.3
Mixing	6,612	6	1,102.0
Spraying	4,698	24	195.8
Mixing	4,000	3	1,333.3
Spraying	1,500	21	71.4

* *The paired mixing and spraying operations represent a single filling and emptying of the spray tank.*

Source: Oudbier et al. (1974).

A study by Stevens & Davies (1981) confirmed these results; the use of dust formulations was found to result in relatively high amounts of respiratory exposure. This experiment studied the potential for captan exposure of workers involved in various aspects of potato planting in the Columbia river basin. People who were monitored for potential dermal and respiratory exposures included workers filling seed dusting machines with captan, workers cutting and sorting potatoes on seed cutting machines in the vicinity of the dusters, a tractor driver planting the treated potatoes and planter observers who rode behind a planter that contained treated seed potatoes. Respiratory exposure as a percent of total exposure was 8.6% for the dusting machine fillers, 7.0% for the workers on the cutting machines, 9.1% for the tractor driver, and 7.7%

for the observers riding the planter. The respiratory exposure to captan is of particular concern, since inhaled material may be absorbed into the blood stream or swallowed. The route of exposure can be essentially eliminated by use of disposable dust respirators, which are lightweight, inexpensive, and offer little resistance to breathing.

The risk of illness attributed to pesticides varies with the type of farm work. For example, a field worker exposed to residues on a crop runs a greater risk of dermal than inhalation exposure; whereas the pilot of an agricultural aircraft is protected from the direct spray but has a high risk of inhaling pesticide vapors (Coutts, 1980). In a study that assessed the exposure of a tractor driver applying captan and chlorothalonil to Florida ornamentals, Stamper et al. (1989) found that the distribution of fungicide on the applicator depended on which spraying device was used; exposures were much larger when the applicator pulled a boom sprayer than when he pulled a span sprayer (50 vs 4.1 μg captan deposited /kg body weight /kg sprayed). The relationship of exposure to work practice was also confirmed by Mumma et al., (1985). They determined dermal and inhalation exposure of applicators and mixer-loaders to the fungicide mancozeb and its decomposition product ETU during field applications by airplanes in Michigan, Minnesota and Oregon; by airblast sprayers in Ohio; and by compressed air sprayers in an Ohio home yard setting. Although considerable variability existed between different persons performing the same task, mixer/loaders were generally exposed the most, especially on the forearms (from 1 to 9.4 mg/body area). Pilots were exposed on an average of 7.2 times less than mixer/loaders, mostly on their hands; tractor driver applicators were exposed 9.7 times less and, as with the mixer/loaders, mostly on their forearms; and home gardeners were exposed 2.5 times less, mostly on the ankles and legs. It was found that protective clothing greatly reduced or eliminated exposure. ETU was almost never detected (limit less than 0.18 mg/body area), and mancozeb was not detected in the urine.

In a study of occupational exposure to the fungicide fosetyl-Al during greenhouse spraying of ornamentals, Fenske et al., (1987) found that mixers experienced a higher rate of exposure (about twice as much) to the neck and face than did applicators. The highest exposure for both activities occurred on the forearms.

Hand exposure represented only 6% of total exposure, while regions protected by clothing contributed to 47% of the total residue measured for mixers and 60% for applicators. Respiratory exposure accounted for 7–9%. The distribution of exposure over the body and the relative importance of dermal and respiratory exposure were strongly influenced by the use of protective equipment (including clothing).

Winterlin et al. (1984) reported that exposure levels of strawberry pickers to captan varied substantially because of their different harvesting methods. While some workers knelt along the ditch between rows and reached over into the strawberry plants, exposing their sleeves and thighs as well as chests to captan-treated foliage, others simply bent over the plants, exposing themselves much less.

In a continuing effort to develop experimental data on the exposure to pesticides of fruit harvesters of different ages, Leffingwell et al. (1985) conducted two studies involving blackberry and raspberry harvesters in benomyl-treated fields. In the blackberry study, where the ages ranged from 7 to 49, a scatter-plot of average glove exposure rate vs. age suggested that hand exposure for young workers was less than that for older workers. However, when the data were normalized for body weight, resulting in an exposure rate expressed in mg/kg/hr, there was no evidence for exposure as a function of age. The same results were derived from the raspberry study, where the ages of those wearing gloves and patch monitors ranged from 9 to 16, and which found residues in much smaller amounts (μg instead of mg).

V. *REENTRY STUDIES*

The determination of dermal exposure to pesticides by fruit and field crop harvesters forms the basis for establishing reentry intervals. These intervals are designed to permit those at the highest exposure risk, agricultural field workers, to reenter pesticide-treated plots without suffering any ill effects (Zweig, 1983). Intervals are normally calculated for pesticide application in fruit orchards, and they vary from 1 to 30 days, depending on the pesticide and fruit (Knaak, 1980). Sulfur (sometimes used as a fungicide), with its capacity to cause eye irritation and dermatitis (generally 1 to 4 days after application, but as late as 3 weeks during mowing operations) (Nigg & Stamper, 1982), may be claimed to have caused the first reentry problem in agriculture (Gunther et al., 1977).

The primary emphasis of reentry studies is the determination of the dislodgeable portion of the pesticide residue present at different intervals after application (Iwata et al., 1979). As one might expect, the duration of dislodgeable residues is influenced by physical and chemical properties of the pesticide, the formulation and local climatic factors. The most critical determinations concern leaf residues since , for example, it is estimated that a mature orange tree has as much as 25 times the amount of leaf surface as fruit surface (Carman, 1973). With the exception of sulfur, fungicides as a class do not present reentry problems as compared to the more acutely toxic insecticides.

The results of a study along the central coastal area of California indicated that residues of captan and its metabolite, tetrahydrophthalimide (THPI), gradually decreased over a period of 14 days after application of the fungicide on strawberries (Winterlin et al., 1984). Acute exposure to captan appears not to pose any health effects; a physician-toxicologist examining strawberry harvesters found no evidence of harm even though they were exposed to relatively high levels of captan on foliage and in the air (Bragg, 1982).

In a search for other factors that might produce more hazardous conditions for workers exposed to crop residues, Staiff et al., (1977) attempted to determine whether the presence of the fungicides maneb or zineb on apple and peach foliage affected the rate of decay of parathion residues and / or the formation of toxic metabolites such as paraoxon. Parathion is an organophosphate insecticide, and it was conceivable that the metals (Mg and Zn) in maneb and zineb might interfere with normal parathion degradation, producing more hazardous conditions for field workers who enter treated areas. Their data indicate that there was no significant effect on parathion decay on apple or peach foliage which had been sprayed with maneb and zineb. The fungicides did not seem to influence the rate of degradation of paraoxon that formed on either apple or peach foliage.

The unpredictability of worker reentry episodes is frustrating for researchers. The number of episodes in one agricultural region may not compare to that in another region. Nigg & Stamper, (1982) cited varying environmental conditions, which should determine regional and crop-specific preharvest intervals (the time a grower must wait after a pesticide application before a crop can be harvested), for adopting flexible reentry intervals.

The use of pesticides, particularly highly toxic fumigants, in greenhouse operations creates the potential for detrimental worker exposure. A number of factors contribute to this. The interior of a greenhouse can be hot and humid. Many tasks require manual labor. Often work is continuous with no seasonal work patterns (Kundiev et al., 1986). It is common practice to fumigate a greenhouse, ventilate it for a few hours, and then permit workers to reenter. Exposure is aggravated when labor involves prolonged and continuous contact with foliar surfaces bearing pesticide residues. In a study of greenhouse reentry intervals it was found that sulfur levels rose to 0.7 mg/m^3 four hours after the beginning of fumigation. After one hour of ventilation they decreased slowly and finally disappeared. Overall, it was found that ventilating a greenhouse for two hours after overnight fumigation with sulfur was adequate to provide safe working conditions (Liesivuori et al., 1988). Waldron

(1985) reported that in studies examining air-borne residues of captan and folpet in greenhouses, the decline in residue levels was not significant two hours following application. However, the levels declined and were nondetectable by four hours.

VI. *HEALTH EFFECTS OF FUNGICIDE EXPOSURE*

In most instances, the health effects reported due to exposure to pesticides are acute effects from exposure to the more acutely toxic materials such as organophosphorus or carbamate insecticides. As a general rule, fungicides have a low mammalian toxicity (a large LD) and are rarely the cause of acute intoxication. Rather it is the possibility of chronic poisoning from exposure to small amounts of fungicides, or their residues, over prolonged periods of time that has sparked concerns over the safety of these pesticides. There are very few reported studies of the effects of long term exposure to small quantities of pesticides and their residues including fungicides and fungicide residues.

As is true of toxicology in general, "the dose makes the poison". Direct contact with copper compounds, for instance, may give rise to itching and burning skin rashes (papulovesicular and eczemoatoid lesions), which on continued contact may result in some degree of tissue death (necrosis). Copper dust or salts splashed in the eye can cause severe inflammation of eyelid mucous membranes (conjunctivitis), excessive fluid in the lids (edema) and even ulceration of the cornea. On the other hand, the EBDCs have not been shown to cause serious acute effects as most applicators have experienced no symptoms other than mild conjunctivitis, inflammations of the nasal mucous membrane, pharynx, or bronchi (rhinitis, pharyngitis and bronchitis, respectively), and insignificant dematitis as a result of heavy exposures (Arena & Drew, 1986). However, Oakley (1988) reported a severe dermatological allergy of an apple orchardist who worked with zineb and mancozeb. Contact allergies to other fungicides (captan, benomyl, thiram, captafol, folpet) occasionally occur as well (Oakley, 1988). Thiram and dodine are moderately severe irritants of the mucous membranes and mild irritants of intact skin, but toxic reactions to captan and captafol, beyond hypersensitive skin reactions have been rare.

Exposures leading to debilitating diseases are also reported in the literature. Ferraz et al. (1988), for instance, reported that chronic exposure to maneb (an EBDC fungicide containing manganese) may produce symptoms and signs of central nervous system manganese intoxication. Such poisoning is a well known hazard to people who work in the manganese mining and processing, steel manufacturing, and dry-

cell battery industries. This study, which was done in Brazil, comparing 50 male rural workers with occupational exposure to maneb with 19 rural workers with little fungicidal exposure, noted a significantly higher prevalence of headaches, fatigue, nervousness, memory complaints, and sleepiness in the exposed group.

Another occupational disease found in the literature is "vineyard sprayer's lung", first described by Pimentel & Marques (1969) and observed in Portuguese rural workers who sprayed vineyards with Bordeaux mixture. It is a disease of the respiratory tract, and its lesions have been reproduced in guinea pigs exposed to Bordeaux mixture, copper oxychloride, and organic fungicides (zineb, maneb, mancozeb and folpet). In addition, liver disease with inclusions of copper was identified in 30 workers who had sprayed Bordeaux mixture for periods varying from 3 to 35 years (mean 18 years) and who were suffering already from vineyard sprayer's lung. The amount of copper inhaled by these workers depended on the concentration of the mixture (1 to 2% copper sulfate), the type of sprayer, and the atmospheric and geographic conditions. Spraying was carried out from 15 to 100 days per year and about 600 liters of mixture were sprayed each day by each worker. Exposure to copper sulfate and the presence of abundant deposits of copper within the liver suggested a relationship between occupational exposure to the fungicide and vineyard sprayer's liver, although the researchers admitted that it was difficult to estimate the true incidence of liver disease produced by copper in vineyard sprayers (Pimentel & Menezes, 1977).

Several studies have also been reported involving human exposure to thiram, an extensively used dimethyldithiocarbamate for both foliar applications and seed treatment. Sivitskaya (1974) described ophthalmologic changes in 50 workers, 20 to 58 years old, who had prolonged occupational contact with thiram. There have also been reports in the 1970's of a type of contact dermatitis possibly resulting from the use of thiram and captafol in tropical developing countries (Fishbein, 1976).

VII. SUMMARY

Fungicides, because of their low acute mammalian toxicity, have not been involved in acute farmworker illnesses. As is true of toxicology in general, "the dose makes the poison", and as a rule, the low amounts of fungicides used don't produce any noticeable detrimental health effects. There are, however, some sensitive individuals who, subsequent to coming into contact with fungicides, have experienced contact allergies.

With the exception of sulfur, fungicides, as a class, do not present problems with reentry to treated areas. The potential for exposure can be influenced by a number of factors including the specific combination of pesticides present as well as climatic properties of a given region. Studies have shown that the highest likelihood of exposure occurs during the mixing and loading operations in preparation for application. Most occupational exposures to pesticides can be reduced or eliminated through education on the use of protective gear and adjustments in working practices. While acute effects from exposure to fungicides are not general occurrences, there is the possibility of chronic effects resulting from prolonged periods of exposure. Further investigations of this possibility would be worthwhile.

APPENDIX A

FUNGICIDES AVAILABLE IN THE U.S.

anilazine (Dyrene)
benalaxyl (Galben)
benodanil
benodil
benomyl (Benlate)
biphenyl (diphenyl)
bitertanol
blasticidin-S
Bordeaux mixture (hydrated lime and copper sulfate)
busan 30A
4-butyl-2H-1,2,4-triazole
cadmium chloride
captafol (Difolatan)
captan (Orthocide)
carbendazim
carboxin
chinosol (8-hydroxy quinoline sulfate)
chloranil
chloroneb
chloropicrin
chloro-6-(2-furanyl-methoxy)-4-(trichloromethyl) pyridine and metabolites
chlorosulfamic acid
chlorothalonil (Bravo)
chlozolinate (Serinal)
copper carbonate (combined copper)
copper hydroxide (kocide, copper kocide)
copper naphthenate
copper nordox (cuprous oxide)
copper oxychloride sulfate
copper sulfate (basic)
copper zinc sulfate
cypendazole
dazomet
DHA (dehydroacetic acid)
dichlone
diclobutrazol (Vigil)
dicloran (botran, DCNA [2,6-dichloro-4-nitroaniline])
dimethirimol
2,4-dinitrophenol
dinocap
diphenylamine
DNOC (4,6-dinitro-o-cresol)
dodemorph acetate
dodine

Duosan
etaconazole
ethirimol
etridiazole (Terrazole)
fenaminosulf (Lesan)
fenarimol (Rubigan)
fenfuram
fenpropimorph
fentin acetate (triphenyltin acetate)
fentin chloride (triphenyltin chloride)
fentin hydroxide (triphenyltin hydroxide)
ferbam
flutriafol (Impact)
fluzilazol (Nustar)
folpet
Fore
formaldehyde
fosetyl-Al (Aliette)
fthalide (Rabcide)
glyodin
guazatine (acetate, Panoctine)
hexachlorobenzene
hexachlorophene
hexaconazole (Anvil)
hexadecyl cyclopropane carboxylate
hypochlorous acid (Clorox, Purex)
imazalil
iprodione
isoprothiolane (Fuji-One)
kasugamycin
kitazin (IBP)
lime sulfur
MAFA (ferric ammonium salt of methane arsonic acid, neo-asozin)
mancozeb
maneb
manganous dimethyldithiocarbamate
mebenil
mepronil
metalaxyl (Ridomil)
metam-sodium
methyl isothiocyanate
methyl thiophanate
metiram
metiram complex (Pallinal)
myclobutanil
nabam
nitrapyrin
nuarimol
octhilinone
ofurace
ortho-phenylphenol and its sodium salt
oxycarboxin
oxythioquinox
PCNB (pentachloronitrobenzene, quintozene)
phenothiazine
piperalin (Pipron)
polyoxin
polyram
prochloraz
procymidone (Sumilex)
propamocarb hydrochloride
propiconazole (Tilt, Banner)
Pseudomonas fluorescens
pyrazophos (Afugan)
sodium and potassium azide
sodium arsenite
sodium azide
sodium diacetate
sodium dimethyldithiocarbamate
sodium polysulfide
streptomycin
sulfur
sulfur and nitrothal-isopropyl (Kumulan)
sulfur dioxide
tetraiodoethylene
thiabendazole
thiophanate
thiophanate-methyl
thiram
tolclofos-methyl (Rizolex)
triadimefon (Bayleton)
triadimenol (Baytan)
tricyclazole
tridemorph (Calixin)
triflumizole
triforine (Funginex)
validamycin A (Validacin)
vinclozolin (Ronilan)
zinc sulfate
zineb
ziram
Zyban

APPENDIX B

FUNGICIDES GROUPED ACCORDING TO ACUTE ORAL RAT TOXICITY

LD_{50} = mg/kg

1–50	
Fentin chloride	18[a]
MEMA	25
MEMC	22–44
mecuric oxide	18
50–100	
blasticidin S–3	55.9–56.8
fenaminosulf	75
hexachlorophene	56–66
100–1,000	
calomel	210
copper hydroxide	1,000
copper oxhchloride	1,000
copper sulfate, basic	1,000
dazomet	640
dinocap	980
fentin hydroxide	156–345
guazatine	227
metalaxyl	669
nabam	395
pyrazophos	415–778
thiram	780
triadimenol	700–1,200
triphenyltin acetate	140–298
triphenyltin hydroxide	156–345
1,000–10,000	
anilazine	5,000
benalaxyl	4,200
bitertanol	5,000
captafol	5,000–6,200
captan	9,000
carboxin	3,820
chinosol	1,200
chloroneb	5,000
copper nordox	1,516
DCNA	5,000
diclobutrazol	4,000

dichlone	1,300	Tilt	1,517
dimethirimol	2,350	triadimefon	1,020–1,855
dodemorph acetate	4,180	tridemorph	1,410
dodine	1,000	zineb	5,200
fenarimol	2,500		
fenpropimorph	4,055	**>10,000**	
isoprothiolane	1,190	benomyl	10,000
Kumulan	9,400	carbendazim	15,000
MAFA	5,700[a]	chlorothalonil	10,000
maneb	7,990	Duosan	10,200
metam-sodium	1,700–1,800	fenfuram	12,900
methyl thiophanate	9,700	ferbam	17,000
ofurace	2,600-3,500	folpet	10,000
ortho-phenylphenol	2,700	fthalide	10,000
oxycarboxin	2,000	iprodione	10,000
PCNB	1,700	Kasugamycin	22,000
phosethyl Al	5,000	mancozeb	11,200
piperalin	2,500	mepronil	10,000
prochloraz	1,600	metiram	10,000
procymidone	6,800–7,700	Pallinal	10,000
propamocarb		polyoxin Al	14,665–14,734
hydrochloride	8,600	thiophanate	15,000
Rizolex	5,000	triforine	16,000
Serinal	4,500	validamycin A	20,000
Terrazole	1,077	vinclozolin	10,000
thiabendazole	3,100	vondozeb	10,000
thiophanate-methyl	7,500	Zyban	10,200

[a] *Oral LD50 for mouse.*

Source: Farm Chemical Handbook (1988).

APPENDIX C

EXAMINATION OF FACTORS INVOLVED IN ASSESSING RISKS FROM PESTICIDE RESIDUES IN FOOD

I. INTRODUCTION

The specific pesticides and the amounts applied to any crop are not arbitrarily chosen. Before any pesticide can be legally applied in the United States (U.S.) it must be registered by the U.S. Environmental Protection Agency (EPA). The specified use patterns are determined by testing the pesticide on each crop in the various regions of production under a variety of application conditions to determine effectiveness as well as how and when to use it. These tests are also used to determine the appropriate number of days that should elapse between the last application and harvest of the crop; this is known as the Pre-Harvest Interval (PHI). All these data are used in an application for registration and, in the case of food crops, petition for tolerance (maximum levels of residues allowed for a pesticide and its significant metabolites or breakdown products) on each specific crop.

Tolerances are enforcement standards based on the pesticide level required in efficacious production of a food crop coupled with

determinations of the safety of that level. They are established through analyses of residue levels found at harvest in different geographical regions. These are the residue levels that result from the maximum number of applications per year at the maximum application rate with the minimum PHI. In considering a petition for tolerance EPA is required to consider the potential health effects of the specific pesticide.

As part of the registration process, EPA reviews a number of required scientific studies submitted by the party seeking registration. For food-use pesticides these studies include:

1. Toxicological investigations
    a. acute, subchronic and chronic toxicity
    b. reproductive effects
    c. teratogenicity (birth defects)
    d. mutagenicity (alteration in the germ line)
    e. carcinogenicity (tumor formation)
    f. pharmacokinetics (absorption, distribution, metabolism and excretion)
    g. eye and skin irritation
2. Environmental fate investigations
    a. surface runoff and leachability
    b. soil adsorption
    c. volatility
    d. residue persistence
3. Effects on non-target organisms
4. Bioaccumulation of the pesticide through the food chain (if such studies are appropriate).

Tolerances are granted under the provisions of the Federal Food, Drug and Cosmetic Act (FFDCA). Section 408 of FFDCA, which is used in setting tolerances on raw agricultural commodities, permits an assessment of the benefits and health risks associated with use of a given pesticide. Section 409, which governs food additives, applies to tolerances for pesticides that concentrate during processing to levels above those permitted on the parent commodity or that are added during processing. Section 409 contains the Delaney Clause, which prohibits any food additive that induces cancer in humans or animals. Thus, there is no provision for the consideration of benefits under Section 409; furthermore, a strict interpretation would not permit the use in processed food of any pesticide that had been classified as a

carcinogen. However, EPA has indicated that, for regulatory purposes, they will consider tolerances for pesticides that have been estimated to present a negligible carcinogenic risk. This is generally considered to be a risk below one in a million.

After evaluation of the risks and benefits associated with the proposed use of the specific pesticide, EPA will grant a registration and approve tolerance levels if the benefits of use outweigh the potential risks to human health or the environment under Sec. 408 of FFDCA or if the risk is negligible under Sec. 409. In addition to the federal registration granted by EPA, most states require registration of pesticides for use within each state. This may be a relatively simple process based on the federal registration, or individual states may choose to exercise their authority to regulate pesticides more rigorously then EPA.

The registrant may now have a label for that pesticide that states the uses approved and the farmer may use it as directed (e.g., rates, method of appplication and PHI) on the specified crops. Both the use directions and tolerance levels are legally enforceable. In addition the label specifies safety procedures to be taken during application and may dictate farm worker reentry intervals (Stimmann, 1988).

New information is continuously generated through scientific research. Thus, the requirements in the registration process may be altered in response to the new information. This process has occurred in a number of cases involving pesticides registered prior to the establishment of current data requirements. As a result, the registration status of such pesticides is reviewed, data needs specified and the risks and benefits are re-examined. Registration and setting tolerances must be viewed as an ongoing process in which there are continuing changes of use and status.

II. ESTIMATING RISKS

The evaluation of health aspects, or risks as they are usually called in the regulatory process, uses the equation:

RISK = EXPOSURE X HAZARD.

The use of the word "hazard" is actually not correct since it has the same meaning as "risk"; "toxicity" would be more appropriate. Thus:

RISK = EXPOSURE X TOXICITY

Regardless of which term is used, the point of the equation is that although a given chemical may be toxic, the risk associated with that chemical depends upon the exposure (or dose).

In the case of pesticide residues in food, the exposure aspect is covered through dietary analysis. Hazards, which are basically considered innate properties of the pesticide under evaluation, are placed in two general categories as far as food uses are concerned: carcinogens and non-carcinogens. For regulatory purposes the term carcinogenicity seems to be used more frequently than the term oncogenicity, which is actually the scientifically appropriate term. Oncogenicity refers to incidence of both benign and malignant tumors; whereas, carcinogenicity technically refers only to malignant tumors. From a regulatory perspective the assumption is made that a benign growth may become malignant, hence the use of the term, carcinogenicity.

The category is determined by the toxicological investigations mentioned earlier, and, the evaluation not only includes the carcinogenicity studies but takes into consideration other studies, such as those examining mutagenicity, which may be associated with carcinogenicity. In both categories most of the assumptions made in the evaluation are the result of extrapolations from animal studies. The enormous uncertainties involved in risk analyses have led to a very conservative approach with the goal of erring on the side of safety. Thus the highest risk estimates are used, and scientists are raising an increasing number of questions regarding the wisdom of such an approach. Scientific data indicate that changes are warranted in the ways assumptions are made. The present risk analysis methodology may be draining resources without improving health safety. As a result, a careful review of this methodology should proceed and the necessary changes made to provide a scientifically realistic analytical procedure.

A. *Dietary Exposure*

In order to assess dietary exposures the cumulative residues to which people will likely be exposed from all the food uses are examined. Consideration should be given to whether the residue occurs on edible or conventionally inedible portions of a crop. Also the nature of consumption of specific crops may be a factor. For example, crops such as hops, mint or parsley might have higher tolerances than wheat, apples or tomatoes. In examining the potential exposure from cumulative residues in the diet, there are a number of factors taken into account; most of these relate to the toxicological data on the pesticide.

Certain assumptions are made about what constitutes an average diet. EPA uses the Tolerance Assessment System (TAS), which is based on USDA's 1977–78 food consumption survey (USDA, 1983). TAS breaks dietary consumption estimates of 376 food types into population subgroups according to sex, race, age and region. It also incorporates

specific consumption estimates for raw and processed food forms for most crops consumed in the U.S. (NAS, 1987b). Food consumption patterns have changed somewhat since the 1977–78 survey; the greatest change is an increase in fresh fruits and vegetables. Changes will be necessary in the values for these foods.

Assumptions are also made about the residue levels that are likely to occur in foods. If tolerance levels are used in estimating health effects, these represent the maximum level of residue allowed and are not representative of actual occurrences in most cases. Any method will overestimate pesticide exposure if it implicitly assumes that a pesticide, or all pesticides, is (are) present at a maximum concentration on all of the commodities allowed during the entire lifetime (70 yrs.) of the consumer. Examination of the variability of the field trial residue data, the distribution of the residue levels between edible and non-edible portions of the commodity, and its fate upon cooking or handling all help to define the true intake better (Frawley & Duggan, 1979). For example the residues of the fungicides thiabendazole, fenpropimorph, imazalil, and prochloraz are found in the pulp (the edible portion) of navel oranges at levels which are only a fraction of the level found in the peel (Lafuente & Toledo, 1985; Lafuente et al., 1986 & 1987), but the tolerance is for the whole orange.

Another source of information on residues of registered pesticides in food is FDA's Total Diet Study, better known as the Market Basket Survey (Study). This effort is designed to estimate the dietary intakes of pesticide residues by eight age/sex groups, from infants to senior citizens (specifically,6–11 mo., 2 yr., 14–16 Female, 14–16 Male, 25–30 F., 25–30 M., 60–65 F., and 60–65 M.). FDA personnel purchase foods from local supermarkets four times a year throughout the United States (Northeast, North Central, South, and West). Each market basket contains 234 individual food items that have been chosen to represent the diet of the U.S. population. The foods are prepared table-ready and then analyzed for residues. Since food preparation often reduces the levels of pesticide residues, the analytical procedures used in the Market Basket Study are modified to increase detection sensitivity above that achieved in regulatory monitoring for enforcement limits. This provides an estimate of the actual amount of pesticide residues consumed in foods as they are usually eaten (e.g., scalloped potatoes, coleslaw, apple pie, bread, lasagna, etc.) Gunderson (1988) provided a detailed account of the continual evolution of and refinements made to this study since its inception in 1961.

B. *Risks From Non-Carcinogenic Hazards*

In assessing risks from pesticides that are not suspected carcinogens, the concept of a threshold level is accepted. In other words, there is a concentration level below which no injury occurs. The types of health effects in this category are viewed as the results of direct chemical injury. Examples include cholinesterase inhibition and birth defects. This threshold level, which is determined in a population of test animals, coincides with a chemical concentration known as the Lowest Observed Effect Level (LOEL). The dose or exposure level that produces no observable or measurable adverse effects on the test population is called the No Observable Effect Level (NOEL); it is usually 3, 5 or 10 times below the LOEL depending on experimental design. NOELs may be determined for chronic, sub-chronic and accute effects.

Tolerance levels are established for non-carcinogenic pesticides that are estimated to result in no appreciable risk. These values are called the Acceptable Daily Intake (ADI) or the recently introduced term, Reference Dose (RfD), which essentially has the same meaning as ADI. The ADI is derived from the NOEL on the basis, extent and quality of toxicology data. If the tolerance request is for a new use of an older pesticide that has many currently registered uses and accompanying tolerances, questions may be raised about exceeding the ADI. ADIs are expressed as the amount of the specific pesticide that will be consumed per amount of body weight per day. They are a fraction of the NOEL, frequently 1%. This 100-fold margin of safety is based on the premise that humans are 10 times more sensitive than the most sensitive animal species tested, and some humans are 10 times more sensitive than the least sensitive humans. The margin of safety may be adjusted also to account for children, elderly, infirm and differences in diet. When the injury used to determine the NOEL is irreversible, such as birth defects, the margin of safety can be more than 100 (usually 500–900 in this case). The margin of safety may be increased to 1000 or 2000 if the toxicology data supporting the NOEL are weak, for example, if the population of laboratory animals is fewer than that currently considered optimum or if the length of the test is less than maximum. In rare cases the margin of safety may be as low as 10 if the NOEL has been determined through direct human data and is a reversible biochemical change without concurrent physiologic effects, such as the onset of cholinesterase inhibition.

Thus, in setting tolerances for pesticides considered non-carcinogenic a number of safety factors are built in to produce what are called conservative risk estimates. These safety factors result from the methodology used in establishing the NOEL and the margins of safety which are used to determine the ADI. A further factor of safety accrues

from the fact that the entire acreage of a given crop in the U.S. is not treated with the subject pesticide, and residues on the portion that is treated are usually (approximately 98% of the time) below tolerance levels.

C. *Risks From Carcinogenic Hazards*

In examining risks from pesticides that are suspected to be carcinogens, a different process is used; risk is calculated as a probability, and there are no margins of safety. This approach is taken by the regulatory agencies in view of the many uncertainties associated with carcinogenesis. The health conservative assumption accepted for regulatory work is that no threshold chemical dose exists for cancer, even though a majority of toxicologists have concluded otherwise.

Very little, if any, reliable data exist on human carcinogenesis resulting from pesticide exposure; therefore, data from animal studies must be used in the evaluation process. EPA provides guidelines on the protocols for these studies (Lamb, 1989). The probability of cancer is determined from long-term feeding studies in two animal species (usually rats and mice) using a range of pesticide doses that increase to the Maximum Tolerated Dose (MTD). MTD is the highest dose of a toxicant that results in toxic effects during chronic exposure without causing death and that doesn't decrease body weight by more than 10%. The EPA has established a cutoff point for the upper limit at 1g/kg body weight/day. The concept of MTD seemingly discriminates against chemicals that are not acutely toxic since large quantities can be fed to animals without killing them. The question is often raised why the animals are dosed at such high levels that greatly exceed the likely human consumption level. The answer usually provided in such cases is that at levels comparable to those in the human diet there would likely be no effects. Questions are also raised about extrapolating data from rodents to humans. Considerable efforts have been made and are continuing in trying to improve the extrapolation procedure between species (Yang et al., 1989).

Within certain limits, cancer dose follows the fundamental maxims of toxicology regarding the dose/response effects. The higher the dose, the higher the frequency of tumors, the higher the number of tumors per animal, and the shorter the period for tumor occurrence. Conversely, the lower the dose, the fewer animals produce tumors, the fewer the number of tumors per animal, and the time for tumor occurrence is longer. It is this property which is used to extrapolate from, for example, 5 tumors per 100 mice to 1 tumor per million. This risk level of one in a million is referred to as the Negligible Risk Level (NRL). In other words,

it is the risk level at which the probability of occurence is so low that it will not happen. The one-in-a-million cancer risk assessment means that for a million persons exposed over a 70-year lifespen, the odds are a million to one against the possibility that they will have cancer as a result of the exposure. Of course, one should be aware that this one-in-a-million is a small addition to the one-in-four (250,000 in a million) cancer probability for the U.S. population (Archibald and Winter, 1990).

The mathematical extrapolation from effects on animals exposed to high doses to humans exposed to low doses is highly controversial. Scientists have continually pointed out that biological phenomena do not conform to linear extrapolations. There are many biological factors that impact the dose response curve. At low doses, for example, a human (or even a mouse) enzyme system may be capable of breaking down the chemical to nontoxic products so there are essentially no effects. At high doses the enzyme system may be saturated and definite effects may be noted resulting from the chemical that is not metabolized. Properties of this nature do not lend themselves to extrapolations from a few points at one end of a scale to the far end where concentrations are orders of magnitude different.

Mathematical models are used to predict dietary cancer risks. Selecting a mathematical model to estimate the relationship between dose and the likelihood of tumor development is quite a challenge. A primary problem, as stated by Winter (pers. comm.), is that "Mathematics is infinite; biology is finite." What this essentially states is that biological processes don't necessarily conform to mathematical extrapolations; this is particularly true in estimating the consequences of low-dose exposures from high-dose data.

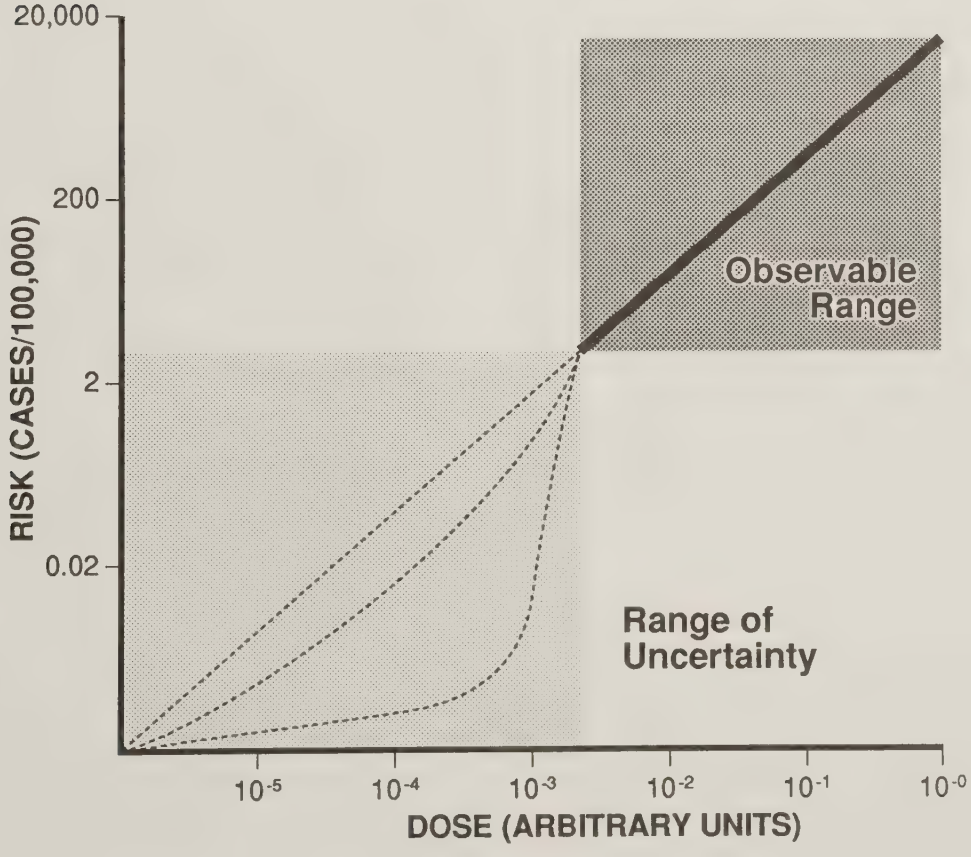
Numerous models have been developed in efforts to more accurately estimate risk. These models usually differ considerably in the low-dose range and present difficulty in assessing the overall variability of risk estimates from multiple experiments (Portier, 1989). The choice of the method of extrapolation of the dose response curve can influence the outcome by as much as a factor of one million (see figure). Current research efforts in this area are directed towards development of models that more accurately reflect biological phenomena.

In generating risk estimates an extrapolation is made using the data from animal studies (see figure). The Y axis represents the change in tumor incidence; the X axis represents the pesticide dose. In the range of uncertainty designated in the figure, the uppermost line, which represents the most conservative approach to risk estimation, is used; the

observable range represents actual data. From this linear extrapolation, which is called the Maximum Likelihood Estimate (MLE), the lower and upperbound 95% confidence limits are produced. The line above the MLE representing the 95% upperbound confidence limit is used by EPA as the dose response curve to determine the oncogenic (carcinogenic) potency of a pesticide. The oncogenic potency, known as Q star or Q*, is the slope of the 95% upperbound confidence limit and represents the change in tumor incidence over the change in dose. Q* is expressed in tumors /mg pesticide /kg body weight/day, and the assumption is made that a person will be exposed to that dose daily for a lifetime (70 yrs.).

Cancer assessment procedures are extremely health conservative; that is, they predict the highest possible risk. This is done to compensate for the many uncertainties in the process. While these risk estimates may be useful for regulatory purposes and for comparing various pesticides, they definitely do not predict actual human cancer incidence (Archibald and Winter, 1990). No mention is made in the regulatory process of estimates made, using other extrapolation models, which are just as likely to occur as the MLE upperbound limit; risk is never expressed as a range that would encompass all estimates.

DOSE-RESPONSE CURVE



This Dose-Response Curve is provided by Mike Ginevan and Paul Roney of RiskFocus

IV. MONITORING FOR PESTICIDE RESIDUES

Realistic risk assessment should relate to the actual levels of pesticide residues found in foods; therefore, monitoring is a vital part of the regulatory process. Pesticide residues in excess of legal limits, or over-tolerance residues, are rare, but can happen for a variety of reasons. They can occur (1) if a crop accumulates pesticides remaining in the soil from an earlier season's treatment, (2) if a pesticide is applied to a crop for which it is not registered, (3) if more than the specified amount is applied, either at one time or over the course of a growing season, (4) if the pesticide is applied closer to harvest thanthe interval specified on the label, (5) if the crop receives drift from another area, or (6) if an unusual weather or edaphic condition permits an increase in uptake or reduces the rate of dissipation. In addition, over tolerance residue may result when pesticides are improperly used (that is, not in accordance with the label) during storage, in warehouses, markets, or restaurants (Stimmann, 1988).

For a pesticide to be present in food, it must either be applied directly to the edible portion of the crop or moved by the plant from its roots or leaves (a systemic or translocatable chemical) to the edible portion. A great many of the pesticides are applied during dormancy (or perennial crops), at pre-emergence, or at early growth stages before fruiting bodies or edible portions begin to form. When pesticides are applied after edible parts begin to form the amount of the residue depends on the surface exposed in relation to the ultimate weight of the plant part, translocations, the rate of breakdown or disappearance of the chemical, and the time to harvest. Pesticides are also used for post harvest treatment so that food crops can be stored as well as shipped without incurring pest contamination. These pesticides are selected specifically for post harvest use and applications should be made so that residues fall within the tolerance levels.

Food commodities are normally sampled at harvest or at various stages of marketing and distribution. Pesticide residues are determined by chemical analysis and expressed as the unit weight of the pesticide per million units weight of the commodity. This is called parts per million (ppm), or for very low values as parts per billion (ppb). Determination of pesticide residues were primarily carried out by colorimetric analysis or bioassay 40 years ago. Today they are primarily conducted by some form of chromatography — gas-liquid chromatography (with many different types of detectors and columns), high performance liquid chromatography, gas-liquid chromatography/mass spectrometry, thin layer chromatography, and plasma chromatography. Formulations are also measured by infrared spectrometry or polarography (Moye, 1981). These developments have reduced the lower limits of detection (LLD)

from a few ppm to as little as a few ppb. In special cases the LLD has been reduced to below parts per trillion into the parts per quadrillion range. These latter levels are not routinely determined in foods.

An analytical chemist does not like to report a result as "zero," out of recognition of the fact that there could be some chemical present at a level below his LLD. Instead they report their "zeros" as "None Detected," or ND and gives the LLD as a footnote. When no residue is detected in a study, the tolerance will be set at the LLD. Since the advent of modern chromatographic methods the LLD is usually about 10 ppb, though it may be higher with some crops when the co-extracted natural plant chemicals are abundant, extensive, impossible to completely "clean up," and interfere with the detection step. The LLD will vary with the crop and chemical. The LLD can usually be raised or lowered by adjusting the sample size and the cleanup procedures. Each lowering of the LLD increases the cost and time devoted to the analysis. Regulatory programs must balance these factors to yield an LLD low enough to provide the information they need, yet not so low that they cannot process the large number of samples they must analyze. In risk assessment, the EPA will calculate the level of residue, when they are reported as ND, as if the chemical had been detected at the LLD, or at one-half the LLD.

V. *SUMMARY*

Before any pesticide can be legally applied in the U.S. it must be registered by the U.S. EPA. In the case of food crops, a tolerance level is established for each registered use. Tolerances are enforcement standards based on the pesticide level required for efficacious production of a food crop coupled with determinations of the safety of that level. In establishing tolerances on raw commodities a benefits and health risk analysis is conducted. Tolerance levels on processed food may be based on negligible risk level, and in such cases benefits are not a consideration. Since new scientific information is continuously generated, registration status and tolerances are reviewed, and the entire process must be viewed as ongoing with continuous changes of use and status.

In order to determine health risks, the potential for exposure and the hazards of the pesticide are examined. In order to assess dietary exposures the cumulative residues from all the food uses are examined. In evaluating hazards, pesticides are divided into two categories as far as food uses are concerned: carcinogens and non-carcinogens. The concept

of a threshold level of safety is accepted for non-carcinogens, and tolerances are established below this level incorporating a margin of safety. For carcinogens, risk is calculated as a probability, and there are no margins of safety. This probability is based on extrapolations from animal data resulting from high doses to the theoretical situation of humans exposed to low doses. These extrapolations incorporate many uncertainties, and the high risk estimates (erring on the side of safety) have raised many questions. The present risk analysis methodology may be draining resources without improving health safety, and as a result, this methodology is under review.

APPENDIX D

DATA FROM CALIFORNIA ROUTINE MONITORING PROGRAM

(POSITIVES ONLY)

Fungicide	*Year*	*Crops*	*# Samples*	*PPM Det*	*Tol*
Anilazine					
	1986				
		celeriac	1	0.68	10
		celery	1	7.65	10
Benomyl					
	1987				
		apple	1	0.1	7
		beans	10	2.75 – 33.4	2
			3	0.6 – 1.6	
		celery	1	2.7	3
		citron	1	27.6	2
		grapefruit	1	3	10
		grapes	7	0.13 – 0.756	10
		nectarines	2	0.78 – 1.4	15
		peaches	2	0.9 – 3.1	15
		plum	1	1.3	15
		prunes	2	0.08 – 0.14	10
		tangerines	1	4.4	10

DATA FROM CALIFORNIA ROUTINE MONITORING PROGRAM (continued)

Fungicide	*Year*	*Crops*	*# Samples*	*PPM Det*	*Tol*
Bordeaux mixture					
	1986				
		nectarines	1	2.52	20
	1987				
		celery	1	25.8	15
Captafol					
	1987				
		tomato	1	1.4	15
Captan					
	1986				
		apricots	3	0.43 – 1.83	50
		beans	1	0.12	25
		blueberries	1	0.3	25
		celery	1	0.55	50
		dewberry	1	0.34	25
		eggplant	1	0.56	25
		grapes	27	0.08 – 4.6	50
		lettuce (leaf)	1	1.17	100
		lettuce (romaine)	1	0.46	100
		nectarines	1	0.43	50
		peaches	2	0.25 – 0.65	50
		raisins	1	1.5	50
		strawberries	9	0.19 – 1.06	25
		tomato	1	0.9	25
		apple	1	0.22	25
		apricots	6	0.68 – 1.05	50
		beans	2	0.29 – 0.32	25
		blackberries	2	1.6 – 1.72	25
		celery	2	0.8 – 1.07	50
		cherries	2	0.2 – 0.24	100
		corn, sweet	1	0.3	2
		grape leaves	1	7.6	50
		grapes	2	50.0 – 105	50
			48	0.12 – 21.26	
		leeks	1	0.13	50
		lettuce (all or unspec)	1	0.19 100	
		lettuce (headtype)	1	21.0	100
		lettuce (leaf)	6	0.55 – 30.2	100
		lettuce (romaine)	3	0.71 – 21.8	100
		nectarines	2	0.26	50
		onions (green)	1	0.2	50
		peaches	1	4.22	50
		pears	3	0.32 – 0.43	25
		potatoes	1	0.3	25
		prunes	1	13.4	50
		raisins	3	0.96 – 1.9	50

DATA FROM CALIFORNIA ROUTINE MONITORING PROGRAM (continued)

Fungicide	*Year*	*Crops*	*# Samples*	*PPM Det*	*Tol*
		raspberries	1	5.6	25
		red raspberries	1	0.42	25
		spinach	1	4.7	100
		strawberries	62	0.044 – 15.94	25
Chlorothalonil					
	1986				
		brussel sprouts	1	0.04	5
		cabbage	10	0.02 – 0.16	5
		cantaloupe	4	0.05 – 1.27	5
		cauliflower	1	0.06	5
		celery	1	32.76	15
			28	0.03 – 12.69	
		cilantro (coriander)	1	0.09	NTE
		cucumber	1	0.02	5
		endive	1	0.05	NTE
		honeydew or honeyball	4	0.02 – 0.3	5
		lettuce (leaf)	2	0.04 – 0.09	NTE
		lettuce (romaine)	4	0.03 – 0.08	NTE
		melons (all or unspec)	2	0.03 – 0.04	
		nectarines	3	0.04 – 0.1	0.5
		onions (green)	2	0.04 – 0.1	0.5
		parsley	7	0.08 – 0.72	NTE
		peaches	2	0.04	0.5
		pears	4	0.03 – 0.04	NTE
		peppers	3	0.04 – 0.13	NTE
		spinach	6	0.02 – 3.73	NTE
		swiss chard	5	5.6 – 16	NTE
		tomatillo (grd. cherry)	1	0.13	5
		tomatoes	39	0.02 – 3.97	5
		zucchini	1	0.21	5
	1987				
		apples	1	0.04	1
		beans	2	0.09 – 0.1	5
		bitter melon	1	0.15	5
		cabbage	1	0.26	5
		cantaloupe	4	0.02 – 0.4	5
		cauliflower	1	0.03	5
		celery	1	35.52	15
			43	0.03 – 5	
		collards	1	0.5	NTE
		cranberries	4	0.027 – 0.28	5
		crenshaw melon	1	0.11	5
		cucumbers	2	0.12	5
		lettuce (leaf)	2	0.03 – 0.07	NTE
		lettuce (romaine)	3	0.06 – 0.1	NTE
		mushrooms	1	1.8	8

DATA FROM CALIFORNIA ROUTINE MONITORING PROGRAM (continued)

Fungicide	*Year*	*Crops*	*# Samples*	*PPM Det*		*Tol*
		nectarines	4	0.02	– 0.05	0.5
		onions (dry)	1	0.06		0.5
		onions (green)	3	0.04	– 0.46	5
		peaches	7	0.03	– 0.07	0.5
		peas	1	0.03		NTE
		peppers (fruiting vegetable)	2	0.04	– 0.05	NTE
		peppers (all or 2 unspec)	2	0.08	– 0.13	NTE
		squash	1	0.07		5
		tomatillo (gr. cherry)	1	0.04		5
		tomatoes	23	0.03	– 1.35	5
		tomatoes (greenhouse)	1	0.05		5
Copper 8-quinolinolate						
	1986					
		kale	1	1.5		6
Copper-zinc sulfate						
	1986					
		celery	1	0.8	15	
Dicloran						
	1986					
		apples	1	0.18		8
		apricots	2	0.68	– 0.96	20
		beans	2	0.11	– 0.46	20
		carrots	6	0.04	– 0.22	10
		celery	44	0.03	– 5.2	15
		cherries	3	0.34	– 2.14	20
		cucumbers	1	0.23		5
		grapes	4	0.08	– 1	10
		lettuce (butterhead)	1	0.16		10
		lettuce (leaf)	1	11.57		10
			6	0.02	– 0.28	
		lettuce (romaine)	2	0.1	– 0.62	10
		nectarines	37	0.07	– 8.2	20
		oriental veg.	1	0.13		15
		peaches	42	0.08	– 13.04	20
		pears	2	0.22	– 0.47	NTE
		peppers (chili-type)	1	3.34		20
		plums	19	0.04	– 8.2	15
		potatoes	1	0.02		0.25
		spinach	1	0.05		NTE
		sweet potatoes	6	2.4	– 7	10
		tomatoes	4	0.05	– 0.65	5
		yams	33	0.03	– 2.65	10

DATA FROM CALIFORNIA ROUTINE MONITORING PROGRAM (continued)

Fungicide	*Year*	*Crops*	*# Samples*	*PPM Det*		*Tol*
	1987					
		apricots	1	6.7		20
		beans	1	0.7		20
		beets	1	0.38		20
		cabbage	1	0.75		10
		carrot tops	4	0.34	– 2.2	10
		carrots	6	0.3	– 1.2	10
		celery	1	25.8		15
			48	0.05	– 1.57	
		cherry	14	0.08	– 0.76	20
		cilantro	1	0.03		NTE
		endive	1	0.06		10
		grapefruit	1	0.06		10
		grapes	4	0.07	– 0.4	10
		kohlrabi	1	0.08		20
		lettuce (butterhead)	1	1.39		10
		lettuce (romaine)	1	0.05		NTE
		mustard (vegetable)	1	0.08		10
		mustard (chinese)	1	1.2		20
		nectarines	62	0.07	– 5.93	20
		peaches	64	0.07	– 15.2	20
		pears	1	0.07		NTE
		persimmons	34	0.05	– 0.18	NTE
		plums	45	0.03	– 3.57	15
		pokeberries	1	0.4		20
		pomegranates	11	0.01	– 1	NTE
		potatoes	2	2.0	– 6.6	0.25
			1	0.1		
		sweet potatoes	20	0.13	– 5.4	10
		tomatillo (gr. cherry)	1	0.57		5
		tomatoes	2	0.06	– 0.08	5
		yams	46	0.05	– 5.3	10
	1988					
		celery	1	65		15
Dinocap						
	1987					
		apples	3	0		1
	1988					
		apples	15	0		1
Folpet						
	1988					
		lettuce (all)	7	0.49	– 11.3	50
			29	0		
		lettuce (head)	2	0.4	– 0.9	50
			5	0		

DATA FROM CALIFORNIA ROUTINE MONITORING PROGRAM (continued)

Fungicide	*Year*	*Crops*	*# Samples*	*PPM Det*		*Tol*
		lettuce (leaf)	1	0.5		50
		lettuce (romaine)	1	1.03		50
		strawberry	1	2.4		25
Mancozeb						
	1987					
		apples	14	0		7
		lettuce	1	0		10
		melons	4	0		4
	1988					
		apples	1	0.88		7
			15	0		
		lettuce	10	0.3	– 6.8	10
		potatoes	4	0.3		0.5
			26	0		
Maneb						
	1987					
		lettuce	2	0.73	– 2.26	10
			3	0		
		peppers	2	0.2	– 0.4	7
		potatoes	1	0		0.1
	1988					
		lettuce	5	0.3	– 4.7	10
			4	0		
		tomatoes	5	0		4
Thiabendazole						
	1988					
		orange	1	3.9		10
Thiophanate						
	1988	almond	1	0		0.2
Thiophanate-methyl						
	1988					
		almond hulls	2	0		1
Triadimefon						
	1987					
		cantaloupe	4	0		0.3
		crenshaw melon	2	0		0.3
		cucumbers	18	0		0.3
		grapes	1	0.25		1
			121	0		
		honeydew	11	0		0.3
		melons, other	5	0		0.3
		pumpkin	1	0		0.3
		squash	1	0.3		0.3
			2	0		

DATA FROM CALIFORNIA ROUTINE MONITORING PROGRAM (continued)

Fungicide	*Year*	*Crops*	*# Samples*	*PPM Det*	*Tol*
		sugar beets	7	0	0.5
		tomatos	75	0	0.2
		zucchini	1	0	0.3
	1988				
		cantaloupe	1	0	0.3
		grapes	3	0.25 – 0.63	1
			32	0	
		melons	4	0	0.3
		squash	4	0	0.3
		sugar beets	7	0	0.5
		tomato	1	0	0.2
Zineb					
	1987				
		oranges	5	0	7
	1988				
		lettuce	5	0	10
		oranges	12	0	7
		potato	1	0	0.5
Ziram					
	1987				
		almonds	17	0	0.1
	1988				
		nectarines	1	0	7
		peaches	4	0	7

Note: NTE = No Tolerance Established for this fungicide on this commodity.

Source: TAS, 1987.

APPENDIX E

DATA FROM CALIFORNIA FOCUSED MONITORING PROGRAM

(POSITIVES AND NEGATIVES)

Fungicide	*Year*	*Crops*	*# Samples*	*PPM Det*		*Tol*
Benomyl						
	1987					
		almonds	2	0		0.2
		almond hulls	59	0		1
		apples	1	0.1		7
			8	0		
		beans	3	0.6	– 1.6	2
			12	0		
		broccoli	11	0		0.2
		cantaloupes	12	0		1
		casabas	1	0		1
		celery	1	2.7		3
			24	0		
		crenshaws	2	0		2
		cucumbers	5	0		1
		grapes	7	0.13	– 0.76	10
			40	0		
		grapefruit	1	3		10
		honeydews	8	0		1

DATA FROM CALIFORNIA FOCUSED MONITORING PROGRAM (continued)

Fungicide	*Year*	*Crops*	*# Samples*	*PPM Det*	*Tol*
		huckleberry	1	0	7
		lemons	7	0	10
		melons, other	2	0	1
		nectarines	2	0.78 – 1.4	15
			11	0	
		oranges	12	0	10
		peaches	2	0.9 – 3.1	15
			21	0	
		plums	1	1.3	15
			17	0	
		prunes	2	0.08 – 0.14	15
			8	0	
		squash	4	0	1
		tangerine	1	4.4	10
		tomatoes	16	0	5
		watermelons	1	0	1
		zucchini	1	0	1
	1988				
		almonds	1	1	1
			9	0	
		apricots	13	0.1 – 0.7	15
			21	0	
		beans	2	0	2
		cantaloupes	24	0	1
		celery	18	0	3
		cherries	2	0.36 – 0.8	15
		grapefruit	4	0	10
		grapes	2	0	10
		melons	5	0	1
		nectarines	28	0	15
		oranges	3	0.57 – 3.9	10
			23	0	
		peaches	4	0.14 – 2.0	15
			20	0	
		plums	2	2.3 – 2.8	15
			34	0	
		squash	3	0	1
		strawberries	1	0.11	5
			26	0	
		tangelos	2	0	10
		tomatoes	4	0	5
Captan					
	1988				
		almonds	1	0.84	2
			10	0	
		grapefruit	2	0	25

DATA FROM CALIFORNIA FOCUSED MONITORING PROGRAM (continued)

Fungicide	*Year*	*Crops*	*# Samples*	*PPM Det*	*Tol*
		grapes	6	0.03 – 1.5	50
			40	0	
		peaches	2	0.11 – 0.17	50
			7	0	
		plums	4	0	50
		prunes	6	0.39 – 1.34	50
			2	0	
		strawberries	10	0	25
Chlorothalonil					
	1988				
		broccoli	2	0.14 – 0.2	5
			10	0	
		brussel sprouts	1	0	5
		cabbage	1	0.15	5
			3	0	
		carrots	5	0	1
		cauliflower	3	0	1
		celery	9	0.19 – 10.0	15
			4	0	
		cucumbers	1	0.21	5
			4	0	
		onions, bulb	1	0.1	0.5
			1	0	
		onions, green	3	0	5
		potatoes	1	0.5	15
			5	0	
		squash	2	0	5
		tomatoes	32	0.08 – 4.7	5
			15	0	
		zucchini	1	0	5
Folpet					
	1986				
		lettuce (butterhead)	1	3.89	50
		lettuce (leaf)	6	1.03 – 24.5	50
		lettuce (romaine)	4	3.26 – 9.15	50
		lettuce, head (unspecified)	1	3.14	50
	1987				
		endive	1	4.5	NTE
		lettuce (all or unspecified)	5	0.8 – 14.48	50
		lettuce (butterhead)	5	0.75 – 19.0	50
		lettuce (head type)	7	0.26 – 7.19	50
		lettuce, leaf	6	0.6 – 43.4	50
		lettuce (romaine)	11	0.8 – 38.4	50

DATA FROM CALIFORNIA FOCUSED MONITORING PROGRAM (continued)

Fungicide	*Year*	*Crops*	*# Samples*	*PPM Det*		*Tol*
Formaldehyde						
	1987					
		celery	1	0.09		Exempt
Iprodione						
	1986					
		corn salad	1	9.49		NTE
	1987					
		grapes	3	0.34	– 0.49	60
		olives	2	0.19		20
Maneb						
	1987					
		lettuce (all or unspecified)	2	0.73	– 2.26	10
		peppers	2	0.2	– 0.4	7
PCNB						
	1986					
		beans (string)	1	0.1		0.1
Sulfur						
	1987					
		grapes	2	0.7	– 1.1	Exempt
Triadimefon						
	1987					
		grapes	1	0.25	1	
		squash	1	0.3	0.3	
Vinclozolin						
	1986					
		basil	3	0.19	– 1.58	NTE
		grapefruit	1	0.08		NTE
		kiwi fruit	1	0.38		10
		mustard (vegetable)	3	0.2	– 1.32	NTE
		rosemary	3	0.17	– 0.95	NTE
		strawberries	17	0.01	– 0.35	10
	1987					
		collards	3	0.37	– 1.54	NTE
		kiwi fruit	6	0.06	– 1.31	10
		onions (dry)	2	0.02	– 0.1	1
		peaches	2	0.08	– 0.99	4
		peppers	1	0.14		3
		strawberries	49	0.05	– 7.18	10
Ziram						
	1987					
		almonds	2	0.12	– 2.00	0.1

Note: NTE = No Tolerance Established for this fungicide on this commodity.

Source: CDFA

APPENDIX F

ADDITIONAL INFORMATION ON PESTICIDE MONITORING BY THE CALIFORNIA DEPARTMENT OF FOOD AND AGRICULTURE (CDFA)

I. INTRODUCTION

The CDFA Chemistry Laboratory Services Branch lists the following criteria that are used to add or remove a pesticide from the screening test:

1) The chemical must be a pesticide (not necessarily only used on food crops).
2) The sensitivity of the analysis must be sufficient to find the chemical at or below the lowest listed tolerance.
3) The minimum detectable level published in the screening list must be attainable by all CDFA residue labs.
4) The pesticide must be determinable on a representative group of registered crops.
5) At least 70 percent recovery of the pesticide residue must be obtained.

6) The length of time required to complete the analysis must be within eight hours.

7) The pesticide analysis must be confirmed by at least two analytical techniques (two different detectors, two different columns, two different methods and mass spectrometry, if possible).

In 1985 a California Assembly bill mandated the Director of the CDFA to expand the pesticide residue monitoring program and include produce destined for processing. In implementing AB 1397, the CDFA contracted with 28 county agricultural commissioners to take samples of produce destined for processing. A total of 1,777 samples were taken of 72 different commodities, 70.3 percent of which were tomatoes, grapes, raisins, apples, lemons, peaches, and oranges. The statistics in the table that follows compare the 1986 and 1987 State Routine Monitoring Programs (produce for fresh market) with the processing program for 1986/87 (July 1986 through December 1987).

RESIDUES OF ALL PESTICIDES IN PRODUCE DESTINED FOR PROCESSING AND PRODUCE DESTINED FOR THE FRESH MARKET (CALIFORNIA)

	Processing Program (1986/1987)	*Routine 1986*	*Fresh Market 1987*
Total number of samples	1,777	5,550	7,010
Percentage of samples with no residues detected	82.7	84.7	79.8
Percent of samples within 50% of tolerance	16.6	12.8	18.7
Percent of samples with illegal residues	0.28	1.9	1.5
Total number of samples with illegal residues	5	105	105

Source: CDFA, 1988.

The five samples found to contain illegal residues in the processing program included the following (CDFA, 1988):

1) A tomato contained detectable residues of profenofos, an insecticide, for which no tolerance had been established. The illegal residue was determined to be caused by pesticide drift and not direct misuse. Profenofos is registered for use on cottonseed at a tolerance limit of 3 ppm. The level detected in the tomato sample was 0.2 ppm.

2) A grapefruit, taken at a processing plant, was found to contain residues of vinclozolin, a fungicide, for which no tolerance had

been established. Vinclozolin is registered for use on such commodities as kiwis, lettuce, and strawberries at a tolerance level of 10 ppm, and on stone fruits at 25 ppm. The grapefruit contained 0.08 ppm.

3 & 4) Two olive samples were found to have illegal residues of chlorpyrifos, for which no tolerance has been established. It was determined that the cause was pesticide drift and a cease and desist order was issued to prevent further harvest. After failed attempts to recondition the olives to eliminate the pesticide drift situation, both the olives in the field and those already harvested were destroyed. Chlorpyrifos, an insecticide, is registered for use on beans, apples, cabbage, and citrus, with tolerance levels ranging from 1 to 2 ppm. Residue levels detected in the olives wee 0.02 and 0.08 parts per million.

5) A fig sample taken prior to the time of harvest was found to contain a residue of chlorpyrifos that was above the legal tolerance limit of 0.1 ppm. A follow-up sample was taken prior to processing in which no detectable residues were found. (The CDFA detection limit for chlorpyrifos is 0.1 ppm.)

The report of the pesticide residue monitoring program stated that, "In viewing the program and statistics, it is apparent that although the residues found do not indicate a problem with produce destined for processing, a continuation of the program is needed to cover major crops not yet adequately sampled, and to monitor specialty crops which have been found to have residue problems in the fresh market monitoring programs." (CDFA, 1988).

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